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Journal:	BMJ Open				
Manuscript ID	bmjopen-2017-019050				
Article Type:	Research				
Date Submitted by the Author:	08-Aug-2017				
Complete List of Authors:	Dasgupta, Paramita; Cancer Council Queensland, Cancer Research Centre Baade, Peter; Cancer Council Queensland, Cancer Research Centre Youlden, Danny; Cancer Council Queensland, Cancer Research Centre Garvey, Gail; Menzies School of Health Research, Epidemiology and Health Systems Aitken, Joanne; Cancer Council Queensland, Cancer Research Centre Wallington, Isabella; Cancer Australia Chynoweth, Jennifer; Cancer Australia Zorbas, Helen; Cancer Australia Youl, Philippa; Cancer Council Queensland, Cancer Research Centre				
Primary Subject Heading :	Epidemiology				
Secondary Subject Heading:	Oncology				
Keywords:	Breast tumours < ONCOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH				
	SCHOLARONE™ Manuscripts				

Variations in outcomes by residential location for women with breast cancer: a systematic review

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Word length:

Manuscript word count (excluding title page, abstract, references, figure legends, and tables): 4640

Abstract word count: 287

References: 104

Tables: 6

Figures: 1

Supplementary files: 3

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Abstract

Objectives: To systematically assess the evidence for variations in outcomes at each step along the breast cancer continuum of care for Australian women by residential location.

Design: Systematic review

Methods: Systematic searches of peer-reviewed articles in English published from 1/1/1990 to 1/3/2015 using PubMed, EMBASE, CINAHL and Informit databases. Inclusion criteria were: population was adult female breast cancer patients; Australian setting; outcome measure was survival, patient or tumour characteristics, screening rates or frequencies, clinical management, patterns of initial care or post-treatment follow-up with analysis by residential location, or studies involving non-metropolitan women only. Included studies were critically appraised using a modified Newcastle-Ottawa Scale.

Results: Fifty-two quantitative studies met the inclusion criteria. Around 60% were considered high quality, 35% moderate and 5% low. No eligible studies examining treatment choices or post-treatment follow-up were identified. Non-metropolitan women consistently had poorer survival, with most of this differential being attributed to more advanced disease at diagnosis, treatment-related factors and socioeconomic disadvantage. Compared to metropolitan women, non-metropolitan women were more likely to live in disadvantaged areas and had differing clinical management and patterns of care. However, findings regarding geographical variations in tumour characteristics or diagnostic outcomes were inconsistent

Conclusions: A general pattern of poorer survival and variations in clinical management for Australian female breast cancer patients from non-metropolitan areas was evident. However, the wide variability in data sources, measures, study quality, time periods and geographical classification made direct comparisons across studies challenging. The review highlighted the need to promote standardization of geographical classifications and increased comparability of data systems. It also identified key gaps in the existing literature including a lack of studies on advanced breast cancer, geographical variations in treatment choices from the perspective of patients and post-treatment follow-up.

Keywords: Breast cancer; Non-metropolitan; Systematic review; Geographical variations; Continuum of care

Strengths and Limitations:

Strengths:

- First systematic review examining evidence for geographical variations in breast cancer outcomes across the continuum of care for Australian women
- Review was conducted according to published guidelines
- All included articles were subject to quality assessment

Limitations:

 Wide heterogeneity across studies in study quality, levels of evidence, methodology, data sources, time period and terminology

• No meta-analysis was possible



Introduction

Worldwide, breast cancer is the most frequently diagnosed cancer among females, accounting for 25% of all new diagnoses in 2012 and is the leading cause of female cancer mortality (15% of total cancer deaths). Among Australian women, breast cancer is also the most common cancer and the second leading cause of cancer mortality. Like other developed countries, Australia has high breast cancer incidence rates but relatively low mortality rates with significant and ongoing improvements in survival, most likely due to earlier detection, screening mammography and improved treatments. However not all women have benefitted equally from these improvements with international studies consistently reporting geographical variations in survival and across the breast cancer continuum of care (such as screening, diagnosis, treatment, post-treatment and psychosocial care). While Australia has relatively high survival rates compared to international benchmarks, significant variations exist with poorer survival for rural and disadvantaged women.

Australia has a universal health-care system, however it is also a country of vast distances with cancer-related services typically being concentrated in major cities¹⁴ so that those living elsewhere often face long travel times and limited access to specialized care.^{11 15} Although about 20% of the total Australian population live outside a major city, for some states and territories this percentage increases to over a third.¹⁶ There is also considerable overlap between remoteness and socioeconomic status with 34% of residents in major cities considered affluent compared to only 2% of those from very remote areas.¹⁷ Current strategies to better address the needs of rural cancer patients and to make cancer care more accessible include the Australian Government's establishment of cancer centres and radiation facilities in regional Australia, exploring innovative models of care and other local-level initiatives.^{15 18}

A comprehensive understanding of the drivers of variations in outcomes across population groups is a prerequisite for ensuring equitable cancer care and improving outcomes for all Australians. This systematic review aimed to identify, assess and synthesize the current evidence relating to geographical variations in survival, patient and tumor characteristics, diagnostic and clinical outcomes for female Australian breast cancer patients. It was conducted as part of a larger systematic review that also investigated psycho-social outcomes¹⁹ and variations by Indigenous status. Such a review may help identify gaps in knowledge, formulate strategic research priorities and develop evidence-based interventions to reduce the observed inequities.

Methods

Terminology

Due to the range of definitions used to define geographical areas, geographical remoteness was categorised into "metropolitan" areas (typically "major cities" or "urban") and "non-metropolitan" areas (comprising the remaining localities). However, where relevant, important patterns observed within the remoteness categories were described in greater detail such as studies relating specifically to remote or very remote areas.

Clinical Questions

The published PRISMA guidelines for conducting systematic reviews²⁰ were followed for this review. As a first step, a series of clinical questions to guide the review were clearly defined and agreed upon before commencing the review process in consultation with a Project Steering Group that included clinicians, researchers, allied health practitioners, consumer advocates with experience in breast cancer and health policy representatives. All questions conformed to PICO guidelines²⁰ in which the target population (P), intervention/exposure (I), comparator (C) and outcomes (O) are clearly defined and used to guide the review process, with the comparator being the only optional component.²¹

Eleven clinical questions examining variations between non-metropolitan and metropolitan women with breast cancer (collectively referred to as 'residential location') were grouped according to 1) survival (one question); 2) patient/tumour characteristics (two questions); and 3) diagnostic and treatment outcomes (eight questions) (Table 1).

Literature searches

The electronic databases: PubMed, EMBASE, CINAHL and Informit were systematically searched for all indexed articles from 1 January 1990 to 1st March 2015. Final searches were undertaken from 2nd to 6th March 2015. The Web of Science database was used for cited reference searches.

Search strategies were based on keywords and subject headings to reflect the review aim with separate queries designed for each clinical question (see supplementary appendix 1). Key terms of 'breast neoplasms', 'female' and 'Australia' were combined with terms relating to geographical aspects including 'rural health', 'geographic inequalities', 'spatial', 'health services accessibility' and 'remoteness' and outcome measures of interest notably 'survival', 'stage', 'diagnosis age', 'socioeconomic', 'mammography', 'screening rate', 're-screening'', 'clinical management', 'patterns of care', 'mastectomy', 'breast reconstruction', 'chemotherapy', 'radiotherapy', 'lymph node' and 'guideline adherence'. Additional synonyms reflecting each of the key terms were also included.

Inclusion criteria

Studies were eligible if they met the following inclusion criteria:

- 1) the population included adult female breast cancer patients or focussed on a breast cancer specific sub-group; and
- 2) had an Australian setting; and
- 3) the outcome measure was survival, patient or tumour characteristics, screening participation or frequency, clinical management, patterns of initial care or post-treatment follow-up; and
- 4) was
 - a) a quantitative study on non-metropolitan versus metropolitan comparisons; or
 - b) a qualitative study on geographical inequalities; or
 - c) quantitative or qualitative studies reporting on relevant outcomes for non-metropolitan women only.

The scope of the review was limited to English language peer-reviewed original research articles. Reviews, editorials, books, conference abstracts and commentaries were excluded, although when identified through the systematic searches their reference lists were examined for relevant articles.

Review process

After removing duplicates, the titles and abstracts of all articles identified during the searches were independently reviewed by two authors (first PD, second PY, DY or PB) for possible inclusion based on their relevance to each clinical question. Discrepancies were clarified through discussion between the two reviewers and if necessary the other reviewers were consulted. Full text versions of all articles of potential relevance were then retrieved for more detailed independent assessment by two reviewers as before. During this process articles were classified as "include" or "exclude" with reasons for exclusion being documented. Reviewer decisions were compared and any disagreements resolved by consensus.

Critical appraisal

The quality of all included articles was critically assessed by two independent reviewers using the Newcastle-Ottawa Scale (NOS),²² a risk of bias assessment tool for non-randomised studies recommended by the Cochrane Collaboration²³ that can be readily tailored for the critical appraisal of quantitative cohort studies.⁹ The NOS assesses studies on six items over five broad perspectives: (a) selection bias; (b) measurement of confounders; (c) outcome assessment; (d) follow-up and (e) adjustments for residual confounders (two items). We extended this tool by incorporating features from other published checklists²⁴ ²⁵ to include three additional items to assess (a) study attrition (missing data), (b) statistical methods and (c) data presentation. Studies were scored according to the extent that they met each of the nine assessed criterion (see supplementary appendix 2) using an ordinal scale to rate the risk of bias as 0 (high), 1 (intermediate) and 2 (low) and the individual item scores then summed to give a total quality score. Instances of major differences in total scores 6

between the two reviewers for individual articles were resolved by consensus and each article was then assigned a summary score (averaged across the two scores). The total average score (range of 0-18) achieved across the nine criterion was categorized as "high" (14-18), "moderate" (9-13.5) or "low" (<9) quality. Studies were not excluded based specifically on their quality rating.

Studies were also classified according to the published levels of evidence for quantitative observational studies from the Australian National Health and Medical Research Council (NHMRC)²⁴ in decreasing order of strength as Level I, Level II, Level III-1, Level III-2, Level III-3 or Level IV.

Data extraction

For all included articles, study characteristics including author(s), publication year, title, population, design and outcomes were recorded in a customized database by one reviewer and subsequently checked by another. Any errors or inconsistencies were resolved after consulting the original source.

Results

Study selection

The steps in the review process are illustrated in a PRISMA diagram (Figure 1). A total of 444 articles were identified across combined databases with an additional 37 citations from other sources. After removing duplicates, an initial pool of 182 articles remained of which 61 were excluded after initial scanning of title/abstracts. Of the 121 retrieved full-text articles, 52 met the inclusion criteria and were considered relevant to at least one of the clinical questions. Excluded studies are listed in supplementary appendix 3, including reasons for exclusion.

Study characteristics

All included articles were quantitative and around 77% used administrative data sources such as population-based cancer registries, screening databases or the non-representative (not population based) National Breast Cancer Audit database which has collected data on about 60% of invasive early breast cancers treated by participating Australian (and New Zealand) breast surgeons since 1998. Remaining studies were based on medical record reviews and cross-sectional surveys.

There was considerable heterogeneity in the definition of non-metropolitan and metropolitan populations. While about half of the included studies used standardized definitions such as the Rural, Remote and Metropolitan Areas (RRMA) system, the Accessibility/Remoteness Index of Australia (ARIA) or ARIA+, or remoteness areas defined by the Australian Standard Geographical Classification,²⁷ others defined non-metropolitan and metropolitan areas based on distances to services, population density or postcodes. Two studies did not provide detailed information regarding the basis of their geographical classification (Table 2).

Around 60% of included studies were graded as high quality, 35% moderate and 5% low quality, with a mean score of 13.0 and range of 6.5-17.0. Key limiting factors for these scores were that around a third (29%) of studies did not use a population-based representative sample, while 21% did not adjust for confounders (including age and socio-demographics). Studies based on reliable and objective data sources (cancer registries) were limited in their ability to control for clinical and treatment factors. The use of highly selective or convenience samples and lack of follow-up also reduced study quality. No studies provided Level I evidence, while more than half (53%) gave Level II evidence, 39% Level III-3 and 8% Level-IV evidence (Table 2).

Key findings

Studies are summarized below according to clinical questions within each of the key themes: 1) survival outcomes, 2) patient/tumour characteristics and 3) diagnostic and treatment outcomes. Several studies reported on multiple outcomes. The emphasis is on whether there was evidence of variations in relevant outcomes by residential location and, if so, the direction and a quantitative estimate of the magnitude of the effect. Given the considerable heterogeneity among studies in terms of their quality, levels of evidence, time period and geographical definitions, we have deliberately interpreted any summary patterns with caution.

Survival Outcomes

There was a consistent pattern of significantly poorer survival (in unadjusted analyses) for women in non-metropolitan areas compared to metropolitan women across 13 (12 high and one moderate quality) of 14 included studies both nationally^{28 29} and at the state-level (Table 3).³⁰⁻⁴⁰ The five-year unadjusted relative survival for female breast cancers was about 2-5% (absolute) lower for non-metropolitan than metropolitan women. The one exception was an early high quality study involving women in New South Wales (diagnosed from 1980-1991) that did not report any survival differential.⁴¹

However, no geographical differential in survival was evident across nine^{29 33-39 41} of twelve studies that also reported survival estimates after adjustment for various combinations of known survival determinants including socio-demographic characteristics, spread of disease, comorbidities and treatment-related factors. The remaining three studies³⁰⁻³² all reported poorer survival for non-metropolitan women even after adjustment.

The adjusted results varied according to the combination of variables included in the statistical models. Two of the three papers that reported significant differentials after adjusting for a measure of stage at diagnosis did not consider comorbidities or treatment-related factors. Of the five studies that adjusted for treatment-related factors, four reported no evidence of a survival differential 35-38

while the finding of a significant difference was likely to be limited to women diagnosed prior to the mid-1990s in the remaining study.³²

Patient and Tumour Characteristics

Patient characteristics

Both of the included high quality studies that reported a positive association between area disadvantage and non-metropolitan residence were based on analysis of 30,299 early invasive female breast cancer cases from the National Breast Cancer Audit (Table 4). 42 43 For example, compared to affluent women, socio-economically disadvantaged women diagnosed with breast cancer were 17 times more likely to live in remote areas (than metropolitan areas) 42 while compared to metropolitan women, those from remote areas were 13 times more likely to live in a disadvantaged rather than more advantaged region. 43

Tumour characteristics

No consistent pattern of variations in tumour characteristics by residential location were evident across the 10 included studies (Table 4). Nationally, one high quality study found that non-metropolitan women were 15% more likely to present with tumours >40mm (versus <30mm)²⁶ while two state-based high quality studies also reported similar patterns,^{44 45} despite using different definitions of advanced disease. However, six others (four high, two moderate quality) showed no differences^{30 36 40 46-48} and one (high quality) that metropolitan women were 11% more likely to present with regional disease than non-metropolitan patients, but equally likely to present with distant tumours.³⁹

Diagnostic and Treatment Outcomes

Studies described here assessed geographical variations in relation to two broad topics: breast cancer screening (Table 5) and treatment (Table 6). The target group for the two screening questions refers to women aged 50 to 69 who were eligible (at the time of this review) for the free population-based national mammographic program in Australia (BreastScreen Australia).⁴⁹

Screening rate

All six of the included moderate quality studies relate to the publicly funded BreastScreen program, as there were no data available to assess variations in private mammography, which provided mixed results. An analysis of self-reported data among 11,200 women nationally found that despite poorer access to mammography services, non-metropolitan women had similar screening rates to metropolitan women, ⁵⁰ consistent with an earlier cross sectional survey. ⁵¹ Two state-based studies however reported higher participation rates in the BreastScreen program for non-metropolitan

women. ^{52 53} In contrast women in the target age group who lived within 10-20 km of a relocatable BreastScreen service were 43% less likely to have attended the service than those residing within a 2 km radius of the service. ⁵⁴ Another study found that non-metropolitan women in the target age group were 39% more likely to report never having had a mammogram through BreastScreen Australia than metropolitan women. ⁵⁵ Screening history, perceived breast cancer risk and knowledge about service location were among key predictors of accessing a relocatable screening service in a study involving only 180 non-metropolitan women. ⁵⁶

Rescreening

Results were inconsistent across the four included studies, with a dependence on the time period of data collection. One early (moderate quality) study showed that metropolitan women had higher rescreening rates through the free national BreastScreen program than non-metropolitan women⁵⁵ whereas among three other studies from 1995 onwards, one (moderate quality) study showed no difference in rescreening rates⁵⁷ and two studies (one moderate, one high quality) showed that non-metropolitan women had higher rescreening rates.^{50 58}

Clinical management

Given there are separate Australian guidelines for clinical management of early ⁵⁹ and advanced stage breast cancer, ⁶⁰ the descriptions of variations in clinical management are categorised accordingly.

A consistent pattern of variations in the clinical management of early breast cancer by residential location was evident across 19 (13 high, five moderate, one low quality) of the 20 included studies with only one moderate quality study finding no variations.

Among 30,299 cases extracted from the National Breast Cancer Audit database, non-metropolitan women were at least five times more likely to have a mastectomy than metropolitan women²⁶ while another study using this database reported that the proportion of mastectomies progressively increased with increasing remoteness.⁶¹ Various state-specific studies reported similar patterns⁶²⁻⁶⁷ although the effect was not always statistically significant.^{63 64} Studies using the National Breast Cancer Audit database also found that non-metropolitan women were 6% less likely to undergo breast conserving surgery⁴² and that the proportion who had breast conserving surgery decreased progressively with increasing remoteness.⁶¹ Similar findings were evident across six other studies.^{36 45 62 68-70}

Two studies based on the National Breast Cancer Audit Database reported that non-metropolitan women were up to 20% less likely to receive adjuvant radiotherapy than metropolitan women. 42 61 Moreover women residing in areas lacking radiotherapy facilities had a higher likelihood (23%) of not receiving radiotherapy than those from regions with such facilities. 61 At the state-level, non-metropolitan women were also less likely to receive adjuvant radiotherapy after breast conserving

surgery in Victoria and Western Australia, 45 although in Western Australia this effect was not statistically significant for metropolitan women. 36

Compared to non-metropolitan women, metropolitan women had a 10% lower risk of unplanned readmissions. Non-metropolitan women were less likely to undergo sentinel node biopsies (SNB), for example 82% of metropolitan women had a SNB compared to 66% of non-metropolitan women. Non-metropolitan women were also less likely to receive hormonal therapy compared to metropolitan women (74.5% versus 84.6%, p=0.006)³⁶ and 13-46% less likely to receive breast reconstruction although adjusted effects were not always significant. Both low surgical caseload (≤10 cases/year) and non-metropolitan treatment centres were also independent predictors of lower immediate breast reconstruction following mastectomy. However there were no geographical variations in rates of axillary node surgery of access to specialist breast care nurses. Compared to metropolitan women, non-metropolitan women were either equally as likely or even more likely to receive adjuvant chemotherapy.

Of the four included studies comprising non-metropolitan women only, one reported that breast care nurses were important in ensuring continuity of care, 77 two found a high level of patient satisfaction with the treatment decision process 78 79 and one found that geographical setting was no impediment to receiving breast conserving surgery or to accessing multidisciplinary care at a single non-metropolitan treatment centre. 80

The only study examining geographical variations in clinical management for advanced breast cancer was one early study that reported no geographical variations in mastectomy rates among women with metastatic disease.⁶²

Recommended clinical management

Six (three high, three moderate quality) of 10 included studies reported geographical variations in guideline-concordant care with non-metropolitan women being less likely to undergo adjuvant radiotherapy, 42 45 61 hormonal therapy 36 or sentinel node biopsies 72 and more likely to experience longer delays in commencing adjuvant chemotherapy. 46 However the other four studies (two high, two moderate quality) found no significant geographical variations in receipt of recommended care. 64 67 68 70

Referral

Non-metropolitan women were less likely to be referred to a radiation oncologist,⁷⁰ and were more likely to experience delays in assessment by a medical oncologist.⁴⁶ Further, in a cross-sectional survey of 70 non-metropolitan women, 42% were referred to another health professional before surgery.⁷⁹ All studies were of moderate quality.

International studies have consistently shown geographical variations in access to high volume surgical care $^{81-83}$ and provided clear evidence that such care is related to improved breast-cancer survival $^{82.84}$ and better concordance with clinical care guidelines. Hence eligible studies that described access to high caseload surgeons were also considered for this clinical question. One high-quality study reported that non-metropolitan women were 9% more likely to be treated locally by low caseload surgeons 26 (defined as ≤ 10 or ≤ 20 cases/year) with similar findings reported by two other high quality studies. $^{36.42}$

Treatment completion

Of the two included studies one found that non-metropolitan women were more likely to complete prescribed chemotherapy than metropolitan women. Another reported that women treated by low caseload surgeons (\leq 20 cases/year) were more likely to decline breast conserving surgery, mastectomy, radiotherapy, axillary surgery and chemotherapy based on data from the National Breast Cancer Audit. Cancer Audit.

The review did not identify any studies examining geographical variations in the specific treatment options offered to non-metropolitan and metropolitan Australian female breast cancer patients, or post-treatment follow-up according to current national guidelines.⁸⁸

Discussion

This review found consistent evidence for variations in survival and clinical management, limited evidence for variations in diagnostic outcomes and inconsistent evidence for variations in tumour characteristics by residential location of Australian female breast cancer patients.

While gaps in the literature limited our ability to draw clear links between identified variations and the drivers of these variations, there was good evidence that poorer breast cancer survival for non-metropolitan women reflects more advanced disease at diagnosis, greater comorbidities and treatment-related factors. According to the recent systematic review by the International Agency for Research on Cancer (IARC)⁸⁹ there is sufficient evidence for the efficacy of mammographic screening in reducing breast-cancer mortality for women aged 50 to 69 years. In Australia, increasing participation for groups with low screening rates can be achieved through the existing and well established population-based national mammographic program (BreastScreen). Targeted strategies are required including thorough engagement and communication with primary care to improve screening participation rates.⁴⁹ While data on screening participation through BreastScreen is readily available, the lack of data on the number of privately screened women precludes an evaluation of actual population-based screening participation. Hence it remains a priority to explore means to combine

data on public and private screening to gain more comprehensive information on total rates of breast cancer screening nationally.

The review found a consistent pattern of geographical variations in patterns of care and lower receipt of optimal clinical management for early breast cancer among non-metropolitan women in Australia. Reasons for these variations likely included limited access to oncological services and multidisciplinary care. It is envisaged that the establishment of Regional Cancer Centres across Australia and integrated cancer networks should improve access to oncological care for regional patients. However the challenge of overcoming barriers to multidisciplinary care in regional areas remains a key issue, especially as multidisciplinary care is widely considered to be the gold standard of cancer car and has been consistently shown to improve breast cancer-related clinical outcomes. As such, initiatives should be implemented to ensure that all women undergo comprehensive multidisciplinary team assessment and that all relevant treatment options are considered.

Australian clinical practice guidelines for the management of early breast cancer recommend post-operative radiotherapy after breast conserving surgery to reduce the risk of local recurrence, adjuvant endocrine therapy and/or chemotherapy where appropriate based on hormone receptor status, ⁹¹ and sentinel node biopsy offered to women with unifocal clinically node negative tumours (≤ 30mm). ⁹² However this review found limited but consistent evidence for geographical variations in receipt of care according to these guidelines. Specifically, non-metropolitan women were less likely to undergo adjuvant radiotherapy, ^{42 45 61} hormonal therapy, ³⁶ or sentinel node biopsies. ⁷² Lower utilization of sentinel node biopsies in non-metropolitan areas may reflect difficulties in obtaining required radiopharmaceuticals for this procedure as well as less relevant training and experience in performing these procedures among general surgeons outside major treatment centres. ⁷² Surgeon-level interventions may be required to help improve sentinel node biopsy rates and hence quality of care and reduced morbidity.

The finding that non-metropolitan women were less likely to receive adjuvant radiotherapy likely reflects variations in access to such facilities. However it should be acknowledged that all included studies were published in the period 1st January 1990 to 1st March 2015 and that some earlier studies may not reflect current practice and/or the impact of improved access to radiation services with the development of new radiotherapy infrastructure in regional Australia over the last five years. ^{15 93} A study published after the review found that breast conserving surgery rates among regional women in the state of New South Wales increased significantly after the opening of a publicly funded local radiotherapy facility in 2013, compared to earlier years when the only options were a local private or publicly funded out-of-areas services. ⁹⁴ Data at the state-level (Victoria, New South Wales) also indicate temporal improvements in the waiting time from specialist consultation to commencing

prescribed radiotherapy (for any cancer)⁹⁵ although these figures are based on the interval from time of radiation oncologist assessment to starting radiotherapy and not from the time of diagnosis. The implementation of routine reporting of waiting times from the time of diagnosis to commencing radiotherapy by geographical location would help identify when and where delays in referral and commencement of treatment occur.

While the review found consistent evidence for variations in breast cancer survival and clinical management, patterns were inconsistent for other outcomes, primarily due to heterogeneity of the included studies or in some cases a lack of studies. A recent study using data from the Australian state of New South Wales published following this review showed that, although survival had improved across population groups, non-metropolitan women continued to experience poorer survival compared to metropolitan women. ⁹⁶ These findings emphasise the importance of Cancer Australia's (Australia's national cancer control agency) work in establishing a national comprehensive system for recording breast cancer stage and clinical management at the population level thereby enabling accurate monitoring of the effectiveness of strategies and initiatives to improve breast cancer outcomes for non-metropolitan women in Australia.

On an international scale, inequities in access to specialised care⁸¹⁻⁸³ and geographical variations across the breast cancer continuum including screening,⁷ stage at diagnosis^{9 97} and patterns of care^{8 86} ⁹⁷⁻¹⁰² are well documented. There is widespread consensus that these variations reflect a combination of socio-economic, demographic and environmental factors including geography, comorbidities, access, treatment and stage at diagnosis that defy easy solutions.^{7-9 82 83 97 101} The persistence of such inequities even for universal (publicly-funded) health-care systems^{7 82 97 99 102} highlights the complexity of the underlying issues.

Limitations

A number of issues made direct comparisons and to some extent interpretation of findings across studies particularly challenging. The assessment of comparability was hampered by the wide variability in study quality, levels of evidence, methodology, data sources, time period and terminology. These issues also prevented meta-analyses being carried out. Many studies were predominantly conducted at the state-level, making the generalisation of findings to the national level difficult. The review also highlighted the need to improve and standardize definitions of geographical location to produce more uniform and reliable remoteness classifications. This would improve data comparability in terms of residential location and hence facilitate more definitive conclusions to be drawn on the strength of the available evidence. Similar concerns have been noted by international reviews on area-level variations in other cancer outcomes.⁸ 103 104

Moreover, many studies had important limitations including selection bias and inadequate follow-up that impacted their quality. While using registry data allows generalizability of findings, such studies cannot comprehensively control for all potential confounders, especially those related to clinical and treatment factors as Australian cancer registries do not routinely collect treatment information.

Considerable efforts were made to conduct a comprehensive search of existing literature on specified clinical questions by searching multiple databases with complex queries and evaluating reference lists of identified articles, published reviews and government reports to find additional articles. However, it is still possible that the search term criteria used could have unintentionally resulted in exclusion of relevant articles. Included articles were also limited to those indexed in the accessed databases.

Conclusions

By examining the current evidence relating to geographical variations in breast cancer outcomes across the continuum of care for Australian women, this review has important implications for clinical practice, service delivery and future research. It has highlighted the gap in knowledge of variations in the treatment of advanced breast cancers, patient decision making and post-treatment follow-up.

While addressing the geographical variations in breast cancer survival and clinical management will require a multifaceted approach, initial efforts could include improving access to and participation in breast screening programs, raising awareness of the benefits of early detection and enabling all women diagnosed with breast cancer to be assessed by a multidisciplinary team that considers all relevant treatment options and have access to best practice treatment. Recognising the heterogeneity of existing studies in terms of geographical coverage and definitions, the establishment of a national comprehensive system for recording breast cancer stage and clinical management would enable accurate monitoring of the success of these initiatives.

Finally, encouraging evidence-based research aimed at better understanding the reasons for geographical variations in breast cancer management and outcomes at each stage of the continuum of care needs to be a priority to inform the development of targeted initiatives to improve survival and quality of life for rural and remote women with breast cancer in Australia.

Funding

This project was funded by Cancer Australia. Dr Philippa Youl is funded by a National Health and Medical Research Council Early Career Fellowship (#1054038).

Conflict of Interest

The authors report no conflict of interest.

Authors Contributions

All authors contributed to the design of the study. PY and PB coordinated the study; PD conducted the literature searches and drafted the manuscript; PD, PY, DY and PB all acted as reviewers and participated in data collection; PY, PB, DY, JA and GG contributed to the initial draft of the manuscript and all authors refined and approved the final version of the paper.

Acknowledgements

The project was commissioned and funded by Cancer Australia. The authors would like to acknowledge the advice of the Project Steering Committee.

Data sharing statement

No additional data are available

Patient consent

Not relevant

Figure legends

Figure 1: Process of inclusion and exclusion of studies for the systematic review

Supplementary files

Supplementary file 1 Database-specific search queries by individual clinical questions.

Additional file 1 lists search queries for the searched databases by each of the individual clinical questions in numerical order.

File name: Supplementary file 1.pdf

Supplementary file 2 Quality appraisal tools for included quantitative studies. Additional file 2 shows the scoring system used for quality appraisal of the included quantitative studies.

File name: Supplementary file 2.pdf

Supplementary file 3 Excluded studies with reasons for exclusion. Additional file 3 lists the excluded studies with reasons for exclusion in alphabetical order by author.

File name: Supplementary file 3.pdf

Table 1: Clinical questions guiding the systematic review

Survival Outcomes

1. In women diagnosed with breast cancer, do non-metropolitan women have poorer breast cancer survival compared to metropolitan women in Australia?

Patient and Tumour Characteristics

- 2. In women diagnosed with breast cancer, do non-metropolitan women have different socio-demographic characteristics compared to metropolitan women in Australia?
- 3. In women diagnosed with breast cancer, do non-metropolitan women have more advanced tumour characteristics compared to metropolitan women in Australia?

Diagnostic and Treatment Outcomes

- 4. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to access breast screening services compared to metropolitan women in Australia?
- 5. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to adhere to recommended breast screening intervals (2 yearly) compared to metropolitan women in Australia?
- 6. In women diagnosed with breast cancer, are there differences in the clinical management between non-metropolitan and metropolitan women in Australia?
- 7. In women diagnosed with breast cancer, are non-metropolitan women less likely to receive the recommended clinical management compared to metropolitan women in Australia?
- 8. In women diagnosed with breast cancer, are non-metropolitan women more likely to experience delays in referral to breast cancer specialist clinicians compared to metropolitan women in Australia?
- 9. In women diagnosed with breast cancer, do non-metropolitan women experience fewer treatment options compared to metropolitan women in Australia?
- 10. In women diagnosed with breast cancer, are non-metropolitan women less likely to complete prescribed treatment compared to metropolitan women in Australia?
- 11. In women diagnosed with breast cancer, are non-metropolitan women less likely to participate in recommended follow-up compared to metropolitan women in Australia?

Table 2: Summary scores, overall grades and Levels of evidence for included studies

Study	Metropolitan/non-metropolitan definition	Score ²	Quality ³	Level ⁴
Adelson et al 1997 ⁶²	Based on health services	15	High	III-3
AIHW 2013 ²⁸	ARIA+ Remoteness Index	14.5	High	II
Azzopardi et al 2014 ⁶¹	ASGC	9	Moderate	II
Baade et al 2011 ⁴⁴	ARIA+ Remoteness Index	16.5	High	II
Barratt et al 1997 ⁵¹	RRMA Classification	9.5	Moderate	II
Bell et al 2012 ⁷³	Postcodes ¹	15	High	II
Bonnet <i>et al</i> 1990 ³⁰	Postcodes ¹	14.5	High	II
Budden et al 2014 ⁷⁸	N/A – regional women only	10	Moderate	IV
Campbell et al 2006 ⁷⁶	Based on place of residence	9.5	Moderate	III-3
Chen et al 2015 ³¹	ARIA+ Remoteness Index	15.5	High	II
Clayforth et al 2007 ³²	Postcodes ¹	15	High	II
Cockburn et al 1997 ⁵⁶	N/A – rural and remote women only	10	Moderate	III-3
Craft et al 1997 ⁶⁸	RRMA Classification	12	Moderate	III-3
Cramb <i>et al</i> 2012 ³³	Distance to radiation treatment facilities	15.5	High	II
Dasgupta et al 2012 ³⁴	ARIA	16.5	High	II
Eley <i>et al</i> 2008 ⁷⁷	N/A- rural and remote women only	7.5	Low	IV
Fox et al 2013 ⁴⁶	RRMA Classification	10.5	Moderate	III-3
Hall & Holman 2003 ⁷⁴	ARIA	14.5	High	II
Hall et al 2004a ³⁵	ARIA	15	High	II
Hall et al 2004b ⁶⁹	ARIA	14.5	High	II
Hill <i>et al</i> 1994 ⁷⁰	Postcodes ¹	12.5	Moderate	II
Hughes et al 2014 ⁵⁷	Postcodes ¹	10.5	Moderate	III-3
Kok et al 2006 ⁴⁵	RRMA Classification	14.5	High	III-3
Koshy et al 2005 ⁶³	Postcodes ¹	9.5	Moderate	III-3
Kricker et al 2001 ⁶⁴	Unclear	16	High	II
Lai et al 2007 ⁷¹	RRMA Classification	15	High	II
Leung et al 2014 ⁵⁰	ARIA+ Remoteness Index	12.5	Moderate	III-3
Lord et al 2012 ⁴⁷	ARIA	14	High	II
Luke et al 2004 ⁴⁸	Postcodes ¹	14	High	II
Martin et al 2006 ⁶⁵	Based on place of residence	14.5	High	II
Mastaglia & Kristjanson 2001 ⁶⁶	Unclear	6.5	Low	IV
Mitchell et al 2006 ³⁶	Postcodes ¹	16	High	II
Morris <i>et al</i> 2012 ⁷²	ASGC	10.5	Moderate	III-3
O'Byrne et al 2000 ⁵⁸	RRMA Classification	15.5	High	III-3
Ristevski et al 2012 ⁷⁹	N/A - regional women only	9	Moderate	IV

Study	Metropolitan/non-metropolitan definition	Score ²	Quality ³	Level ⁴
Roder et al 2012a ²⁹	ASGC	14.5	High	III-3
Roder et al 2012b ⁸⁷	ASGC	14	High	III-3
Roder et al 2013a ⁴²	ASGC	14	High	III-3
Roder et al 2013b ²⁶	ASGC	14.5	High	III-3
Roder et al 2013c ⁷⁵	ASGC	14.5	High	III-3
Roder et al 2014 ⁴³	ASGC	15	High	III-3
Schofield et al 1994 ⁵⁴	Distance to screening services	10.5	Moderate	II
Siapush & Singh 2002 ⁵⁵	Based on residential area	12.5	Moderate	II
Spilsbury et al 2005 ³⁷	Postcodes ¹	16	High	II
Sullivan et al 2003 ⁵²	Postcodes ¹	11	Moderate	III-3
Supramaniam et al 2014 ³⁸	ARIA+ Remoteness Index	17	High	II
Taylor 1997 ⁴¹	(1) 16 regional areas (2) capital city, other metropolitan, rural	14.5	High	II
Thompson et al 2008 ⁶⁷	ARIA+ Remoteness Index	14.5	High	II
Tracey et al 2008 ³⁹	ARIA	15	High	II
Tulloh & Goldsworthy 1997 ⁸⁰	N/A - all from rural and remote areas.	7	Low	III-3
Weber et al 2014 ⁵³	ARIA+ Remoteness Index	10.5	Moderate	III-3
Wilkinson & Cameron 2004 ⁴⁰	Postcodes ¹	9.5	Moderate	II

ARIA Accessibility/Remoteness Index of Australia; ASGC Australian Standard Geographical Classification; N/A Not applicable; RRMA Rural, Remote and Metropolitan Areas

- 1. Postcodes within state capital were considered metropolitan, remaining were non-metropolitan
- 2. Average score over scores from two independent reviewers. Please refer to text for further details.
- 3. Quality categories: High (score14-18), Moderate (score 9-13.5) or Low (score <9); please refer to text for further details
- 4. Australian National Health and Medical Research Council (NHMRC) ²⁴ levels of evidence in decreasing order of strength are Level II, Level III, Level III-1, Level III-2, Level III-3 and Level IV.

Table 3. Characteristics of included studies on survival outcomes

Study	Location ¹	Design	Source	Period (follow- up)	Sample ²	Outcomes	Analysis	Results
AIHW 2013 ²⁸	National	Cohort	ACD	1982-2007 (end 2010)	NS	5-year relative survival	Relative survival	Poorer survival for remote/very remote women (84% versus 90% major cities). ³
Bonnet <i>et al</i> 1990 ³⁰	SA	Cohort	SA CR	1980-1986 (end 1988)	2,565	5-year relative survival	Proportional hazards regression	Poorer survival for non-metropolitan women (74% versus 76-78% metropolitan). They had significantly poorer (p<0.05) survival (2-9 times higher mortality risk) after adjustment. ⁴
Chen <i>et al</i> 2015 ³¹	NSW	Cohort	NSW CCR	2000-2008	36,867	5-year BC specific- survival	Kaplan-Meir, stratified Cox regression (spread of disease)	Poorer survival for outer regional women with regional (82% versus 86% metropolitan) and distant (33% versus 44%) disease. Outer regional women also had significantly (p<0.05) poorer survival (regional: 22%; distant: 30% higher BC mortality) after adjustment. ⁵
Clayforth et al 2007 ³²	WA	Cohort	WA CR	1989, 1994, 1999 (to 2005)	1,729	5-year overall survival	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women (79% versus 85% metropolitan, p=0.014). Metropolitan women had significantly (p<0.001) better survival (30% lower BC mortality) after adjustment. ⁶
Cramb <i>et al</i> 2012 ³³	Qld	Cohort	Qld CR	1996-2007	25,202	5-year relative survival	Bayesian spatial regression	Poorer survival for women living >6 hours from a radiation facility (83% versus 86% living <2 hours, p<0.001). No statistically significant difference after adjustment.
Dasgupta et al 2012 ³⁴	Qld	Cohort	Qld CR	1997-2006 (end 2007)	18,568, first primary, aged 30-79 years	5-year BC specific-survival	Kaplan-Meir, Multilevel regression	Poorer survival for remote/very remote women (88% versus 91% metropolitan, p=0.022). No statistically significant (p=0.366) difference after adjustment. ⁸
Hall <i>et al</i> 2004a ³⁵	WA	Cohort	WA Record Linkage Project	1991-2001	7,117, BC- surgery	5-year overall survival	Chi-square, Cox regression	Poorer survival for very remote women (78% versus 83% metropolitan). No statistically significant difference after adjustment. 9
Mitchell et al 2006 ³⁶	WA	Cohort	WA CR	1999 (end 2004)	899, first primary, histologically verified	5-year overall survival	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women (78% versus 87% metropolitan, p=0.001). No statistically significant difference after adjustment. 10
Roder <i>et al</i> 2012a ²⁹	National	Cohort, data linkage	BS Australia, state cancer registries	1991-2006	62,082, screening history (BS Australia)	5-year overall & BC specific survival	Cox regression	Poorer survival for regional non-Indigenous (88-89% versus 90% metropolitan) and Indigenous women (75-79% versus 86%). No statistically significant difference after adjustment. ¹¹
Spilsbury <i>et</i> al 2005 ³⁷	WA	Cohort	WA Record Linkage Project	1982-2000	11,445, BC- surgery	5-year relative & BC specific survival	Relative survival, Cox regression	Poorer survival for non-metropolitan women (82% versus 86% metropolitan, p<0.001). No statistically significant (p≥0.05) difference after adjustment. ¹²
Supramaniam	NSW	Cohort,	NSW CCR,	2001-2007 (end	27,850, aged	5-year BC	Cox regression	Inner regional and rural women had (unadjusted) 11% and

Study	Location ¹	Design	Source	Period (follow- up)	Sample ²	Outcomes	Analysis	Results
et al 2014 ³⁸		data linkage	NSW APDC	2008)	≥18 years	specific- survival		20% poorer survival respectively than metropolitan women. No statistically significant (p=0.703) difference after adjustment. ¹³
Taylor 1997 ⁴¹	NSW	Cohort	NSW CCR	1980-1991 (end 1992)	25,793	5-year relative survival	Relative survival models	No statistically significant ($p \ge 0.05$) differences in either unadjusted or adjusted ¹⁴ survival estimates by residential location.
Tracey et al 2008 ³⁹	NSW	Cohort	NSW CCR	1980-2003 (end 2004)	59,731, known spread of disease	Case fatality: 5 and 10 years post-diagnosis	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women than metropolitan women. No statistically significant (p≥0.05) difference after adjustment. ¹⁵
Wilkinson & Cameron 2004 ⁴⁰	SA	Cohort	SA CR	1977-1993 (to 2000)	NS	5-year BC specific- survival	Survival percentages	Poorer survival for non-metropolitan women (73% versus 77% metropolitan). ³

not stated

- 1. National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia and WA Western Australia
- Female invasive breast cancers cases
- 3. No adjusted analyses
- Adjusted for tumour size and nodal status.
- Adjusted for age at diagnosis and stratified by spread of disease (classified as localised, regional or distant).
- Adjusted for age and year at diagnosis, clinical features, surgical caseload and treatment related factors.
- Adjusted for age at diagnosis, spread of disease, distance to treatment and area-disadvantage.
- Adjusted for age at diagnosis, Indigenous status, socio-demographic factors, spread of disease and area-disadvantage.
- Adjusted for age and year at diagnosis, Indigenous status, socio-demographic factors, comorbidities, area-disadvantage, hospital related factors and surgical type.
- 10. Adjusted for age at diagnosis, clinical features, surgical caseload and treatment related factors.
- 11. Adjusted for age at diagnosis, diagnostic period, Indigenous status and area-disadvantage.
- 12. Adjusted for age at diagnosis, diagnostic period, Indigenous status, comorbidities, area-disadvantage, hospital type and treatment related factors.
- 13. Adjusted for age and year at diagnosis, Indigenous status, comorbidities, area-disadvantage, spread of disease and surgical type.
- 14. Adjusted for age at diagnosis, spread of disease, follow-up interval and interactions between these variables.
- 15. Adjusted for age at diagnosis, diagnostic period, spread of disease, area-disadvantage and country of birth

Table 4. Characteristics of included studies on patient and tumour characteristics

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
Roder <i>et al</i> 2013a ⁴²	National	Non- representative sample	NBCA database ³	1998-2010	30,299, early disease ⁴ , residential postcodes noted	Predictors of increasing residential remoteness for women with BC	Chi-square, Logistic regression	Disadvantaged women (versus affluent) significantly (p<0.001) more likely to live in inner regional (10 times), outer regional (33 times) or remote areas (17 times) than metropolitan areas. Residential disadvantage a key predictor of increasing remoteness
Roder <i>et al</i> 2014 ⁴³	National	Non- representative sample	NBCA database ³	1998-2010	30,299, early disease ⁴ , residential postcodes noted	Predictors of lower residential socioeconomic status for women with BC	Chi-square, Logistic regression	after adjustment. ⁵ Low socioeconomic status significant (p<0.001) predictor of non-metropolitan residence. Inner regional (five times, versus metropolitan), outer regional (10 times) and remote women (13 times) significantly more likely to live in disadvantaged than affluent regions after adjustment. ⁶
Baade <i>et al</i> 2011 ⁴⁴	Qld	Cohort	Qld CR	1997-2006	18,568, aged 30-79 years, known tumour size and nodal status (if ≤20mm)	Stage ⁷	Multilevel logistic regression	Outer regional women 13% (p<0.001) more likely to present with advanced disease than metropolitan women after adjustment. ⁸
Bonnet <i>et al</i> 1990 ³⁰	SA	Cohort	SA CR	1980-1986	1,171, known tumour size and nodal status	Tumour size, nodal status	Chi-square	No statistically significant (p>0.10) differences in tumour size or nodal status by residential location.
Fox et al 2013 ⁴⁶	NSW	Medical chart reviews	Records (4 medical centres)	2008-2011	400, Stage 1-III, had adjuvant CT, consulted medical oncologist	Median tumour size, grade, receptor status, nodal status	Chi-square, Mann- Whitney	No statistically significant differences in tumour size by residential location. Nonmetropolitan women significantly (p ≤0.01) more likely to have triple negative, low grade or greater nodal spread tumours.
Kok <i>et al</i> 2006 ⁴⁵	Vic	Retrospective cohort	BS Vic	1993-2000	5,294 diagnosed through screening	Tumour size, nodal status	Chi-square	Non-metropolitan women had larger tumours (10-19mm: 49% versus 47% metropolitan; >20mm: 25% versus 23%, p<0.001); no statistically significant (p≥0.05) difference in nodal status by residential location.
Lord <i>et al</i> 2012 ⁴⁷	NSW	Cohort	NSW CR	2001-2002	6,664, non-metastatic, known spread of disease	Degree of spread ⁹	Chi-square	No statistically significant (p=0.08) difference in degree of spread by residential location.
Luke <i>et al</i> 2004 ⁴⁸	SA	Cohort	SA CR	1997-2002	4,912, known tumour size	Large tumour (≥30mm)	Mann- Whitney	No statistically significant (p=0.130) difference in tumour size by residential location.
Mitchell et	WA	Cohort	WA CR	1999	899, first primary,	Tumour size, grade,	Chi-square	No statistically significant (p≥0.103)

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
al 2006 ³⁶					histologically verified	vascular invasion,	·	differences in tumour size or other clinical
						nodal status		characteristics by residential location.
Roder et al	National	Non-	NBCA	1998-2010	30,299, early disease ⁴ ,	Tumour size, grade,	Chi-square,	More remote women (outer-regional,
$2013b^{26}$		representative	database ³		residential postcodes noted	vascular invasion,	Mann-	remote/very remote areas combined) 15%
		sample				receptor status,	Whitney	(p=0.005) more likely to present with larger
						nodal status		tumours (>=40mm versus <30mm) than
								metropolitan women. No statistically
								significant (p≥0.046) differences in other
								clinical features by residential location.
Tracey et al	NSW	Cohort	NSW CCR	1980-2003	59,731, known spread of	Degree of spread ⁹	Logistic	Metropolitan women 11% more likely to
2008 ³⁵					disease		regression	present with regional disease than non-
								metropolitan women after adjustment. ¹⁰
								Difference not statistically significant
								$(p \ge 0.05)$ for distant disease.
Wilkinson &	SA	Cohort	SA CR	1980-1998	NS	Proportion of	Chi-square	No statistically significant difference
Cameron						tumours >20mm		(p=0.57) in tumour size by residential
2004^{40}								location.

BS BreastScreen, CR Cancer Registry, CCR Central Cancer Registry CT Chemotherapy, NBCA National Breast Cancer Audit Database, NS not stated

- 1. National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia; Vic: Victoria and WA Western Australia
- 2. Female invasive breast cancers cases
- National Breast Cancer Audit Database covers about 60% of early (note 4) invasive female breast cancers diagnosed in Australia between 1998 and 2010.
- 4. Early disease defined as invasive tumours of ≤50mm diameter with either impalpable or palpable but not fixed lymph nodes and no evidence for distant metastases.
- 5. Adjusted for age at diagnosis, diagnostic period, area disadvantage, annual surgeon caseload, treatment centre location and treatment-factors.
- 6. Adjusted for diagnostic period, referral source, tumour laterality, ovarian ablation and treatment centre location.
- Classified as early (\(\le 20mm\) size, no evidence of nodal involvement) or advanced (\(\re 20mm\) size and/or positive nodal status, includes cases diagnosed due to metastatic disease)
- Adjusted for age at diagnosis, diagnostic period, Indigenous status, socio-demographic factors and area-disadvantage.
- Classified as localised (node-negative confined to breast tissue), regional (involves regional lymph nodes or adjacent tissues, includes locally advanced disease) or distant (spread to distant organs or lymph nodes, includes metastatic disease)
- 10. Adjusted for age at diagnosis, diagnostic period, area-disadvantage and country of birth

Table 5. Characteristics of included studies on diagnostic outcomes

Study	Location ¹	Design	Source	Period	Sample	Outcomes	Analysis	Results
Barratt <i>et al</i> 1997 ⁵¹	National	Cross- sectional	Electronic white telephone directory	1996	2,935 randomly selected women, aged 30-69 years, no breast cancer history.	Self-reported screening mammography history	Chi-square	No statistically significant (p ≥0.05) differences in percentage of women aged 50-69 years (n=1,035) who reported having a screening mammography by residential location.
Cockburn et al 1997 ⁵⁶	Vic	Cross- sectional (Local media, community groups (in target rural area)	1995	180 women, aged 50- 69 years, understood spoken English, no screening history 6 months pre-interview	Utilization of a screening mammography service	Logistic regression	50% of sample used service. No previous screening history, higher perceived breast cancer risk, lower education, intention to attend and knowledge of service location all significant predictors (p<0.05) of utilizing it after adjustment. ²
Leung <i>et al</i> 2014 ⁵⁰	National	Longitudinal prospective survey	ALSWH	2001-2010	11,200 women, from 1946-1951 birth cohort, aged 50-55 years (2001)	Self-reported screening mammography history, rescreening (within last two years)	Chi-square, Logistic regression	No statistically significant (p≥0.05) differences in screening rates by residential location after adjustment. ³ Non-metropolitan women had significantly (p<0.001) poorer adjusted access to screening services. They were 25-63% (p<0.05) more likely to have been rescreened than metropolitan women. ³
Schofield et al 1994 ⁵⁴	Vic	Random sampling	Electoral lists (women from target area)	1988-1990	668 women, aged 50-69 years	Utilization of a single screening mammography service	Logistic regression	Women who lived within 10-20 km of the service 43% (p<0.05) less likely to have accessed it than those residing within 2km of it after adjustment. ⁴
Siapush & Singh 2002 ⁵⁵	National	Multistage sampling	ANHS	1995	Subsample of 10,179 women, aged ≥18 years	Self-reported screening mammography history, rescreening (within a year if aged ≥50-years)	Logistic regression	Non-metropolitan women 39% (p<0.001) more likely to report no screening mammography history and 20% (p<0.05) more likely to not have been rescreened than metropolitan women after adjustment. ⁵
Sullivan et al 2003 ⁵²	WA	Data linkage	Disability Services database, WA CR, BS WA	1982-2000	380 women, aged 50- 69 years, known intellectual disability, matched to CR and BS databases	Utilization of screening mammography service	Logistic regression	Non-metropolitan women 2 times (p<0.05) more likely to have utilized the free screening mammography programme than metropolitan women after adjustment. ⁶
Weber <i>et al</i> 2014 ⁵³	NSW	Cohort	Medicare Australia	2006-2010	101,063 women (77,139 Australian,	Self-reported mammography	Poisson regression	No statistically significant differences in screening rates among immigrant women

Study	Location ¹	Design	Source	Period	Sample	Outcomes	Analysis	Results
					23,024 immigrant), aged ≥50 years, included in the 45 and Up Study	screening		but among Australian-born women, those from non-metropolitan areas were 2% more likely to have utilized the national screening program than metropolitan women after adjustment. ⁷
Hughes <i>et al</i> 2014 ⁵⁷	WA	Retrospective cohort	BS WA	1999-2008	Number unknown, aged 50-67 years, initial screen (BS WA)	Rescreening (within 27 months of initial screen) ⁸	Not stated	No statistically significant differences in rescreening rates by residential location.
O'Byrne <i>et al</i> 2000 ⁵⁸	Vic	Retrospective cohort	BS Vic	1995-1996	121,889 women, aged 50–69 years, initial screen (BS Victoria), invited for a routine biennial screening mammogram	Rescreening (within 27 months of initial screen) ⁸	Logistic regression	Non-metropolitan women were 13-24% more likely to return for routine rescreening than metropolitan women after adjustment. ⁹

ALSWH Australian Longitudinal Study on Women's Health, ANHS Australian National Health Survey, BS BreastScreen, CR Cancer Registry

- 1. National: all states/territories; NSW: New South Wales; Vic: Victoria and WA Western Australia
- Adjusted for screening history, perceived breast cancer risk, education, breast-cancer screening awareness, perceived barriers, knowledge of service location, intention to attend, social influences, socio-demographic factors and access issues
- 3. Adjusted for time and interaction between time and residential area
- 4. Adjusted for intention to attend, experience of, perceived susceptibility to, concerns and knowledge about breast cancer, screening concerns, other preventive behaviour, health related character traits, access and socio-demographic factors.
- 5. Adjusted for age, socio-demographic factors, area-disadvantage and country of birth
- 6. Adjusted for age, marital status, institutional care, level of intellectual disability and medical history
- 7. Adjusted for age, family cancer history, socio-demographic factors and hormone replacement therapy, stratified by place of birth
- Screening interval of 27 months used of recommended 24 months to allow for potential delays in screening availability and data transfer.
- 9. Adjusted for age, Indigenous status, language spoken at home, area-disadvantage, hormone replacement therapy, family breast cancer history and characteristics related to initial screening (recruitment method, type of service attended, symptoms and assessment status)

Table 6. Characteristics of included studies on treatment outcomes

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
Adelson et al 1997 ⁶²	NSW	Retrospective data linkage	NSW CCR, ISC	1991-1992	4,038, known spread disease, BC-surgery	BCS versus MST	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 2 times more likely to have MST (localized disease); adjusted difference not statistically significant (p≥0.05) for metastatic disease. ³
Azzopardi et al 2014 ⁶¹	National	Clinical audit	NBCA database ⁴	1998-2012	21,643, early disease ⁵	BCS versus MST, adjuvant RT (yes/no)	Chi-square (surgical type), Logistic regression (RT)	Proportions of BCS decreased and MST increased significantly (p<0.001) with increasing remoteness Women from areas lacking a RT facility (versus RT facility present) and non-metropolitan women (versus metropolitan) 23% (p<0.001) and 20% (p=0.002) less likely respectively to have RT after adjustment. ⁶
Bell <i>et al</i> 2012 ⁷³	Vic	Longitudinal cohort ⁷	Health & Wellbeing After BC study	2004-2006	366, prior unilateral MST, known BR status	BR (yes/no)	Logistic Regression	Non-metropolitan women 73% (p<0.001) less likely to have BR than metropolitan women after adjustment. ⁸
Budden <i>et al</i> 2014 ⁷⁸	Qld	Cross-sectional	3 regional locations	NS	104, Stage 1-IIA, MST or BCS/RT	Satisfaction treatment decision	Chi-square	90% women satisfied with decision process, 94% with outcome and 69% offered treatment choices.
Campbell <i>et</i> al 2006 ⁷⁶	National (not Tas)	Cross-sectional	State Cancer Registries	1997	544, early disease	Systematic SBN care (yes/no)	Chi-square	No differences in receipt of systematic SBN care (p=0.280) by residential location.
Craft <i>et al</i> 1997 ⁶⁸	National	Retrospective survey	Medicare Australia	1993	4,683, had BC- surgery (on MBS)	Frequency (BCS, AS)	Chi-square	Non-metropolitan women (versus metropolitan) had lower BCS (34% versus 42%, p<0.001); no differences in AS rates by residential location.
Eley <i>et al</i> 2008 ⁷⁷	Qld	Cross-sectional	Non- metropolitan, offered BCN support	2005-2006	51, aged 38-79 years, post active treatment	Interactions with BCN	Frequencies	BCN valuable source of treatment-related information (86% sampled women) and help during decision-process (71%).
Fox <i>et al</i> 2013 ⁴⁶	NSW	Medical chart reviews	Records (4 medical centres)	2008-2011	400, non- metastatic, had adjuvant CT	Delays (consultation medical oncologist, start CT), CT finish	Chi-square, Mann- Whitney	Non-metropolitan women (versus metropolitan) significantly (p<0.001) more likely to have longer consultation and CT start delays and to complete CT course (90% versus 82%, p=0.020).
Hall & Holman 2003 ⁷⁴	WA	Cohort	WA Record Linkage Project	1991-2000	7,303, prior MST or BCS	BR (yes/no)	Chi-square, Cox regression	Non-metropolitan women (versus metropolitan) 46% less likely to have BR, but adjusted difference not statistically significant.
Hall <i>et al</i> 2004b ⁶⁹	WA	Cohort	WA Record Linkage Project	1991-2000	7,304, had BCS or MST	BCS versus MST	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) less likely to have BCS, but adjusted difference not statistically significant. ⁹

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
Hill <i>et al</i> 1994 ⁷⁰	Vic	Population- based survey	Vic CR	1990	856, had BC- surgery, treating surgeon sent questionnaire (patterns of clinical care)	BCS, adjuvant RT, CT, HT (all yes/no), Referral (% patients)	Chi-square, ANOVA, Student t- test	Non-metropolitan women (versus metropolitan) less likely to have BCS (33% versus 46% metropolitan); no differences in adjuvant therapies (no quantitative data) or medical oncologist referrals. 60 women who saw metropolitan (versus non-metropolitan surgeons) more likely to have BCS (48% versus 27%). Non-metropolitan surgeons less likely to refer patients to radiation oncologists (28% versus 43%).
Kok <i>et al</i> 2006 ⁴⁵	Vic	Retrospective cohort	BS Vic	1993-2000	5,294 diagnosed through screening	BCS versus MST, adjuvant RT (yes/no)	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) significantly (p<0.001) less likely to have BCS (58%) and RT after BCS (27%) after adjustment. ¹⁰
Koshy <i>et al</i> 2005 ⁶³	NSW, ACT	Prospective audit	Pathology reports, medical charts, clinicians	1997-2002	1,069, non- metastatic, had BC-surgery	BCS versus MST	Chi-square	Non-metropolitan women more likely to choose MST (23% versus 15% metropolitan) but difference not statistically significant (p=0.09).
Kricker <i>et al</i> 2001 ⁶⁴	NSW	Data linkage	NSW CCR, ISC	1992, 1995	2,020 or 2,883 had BCS or MST	BCS versus MST, AS (yes/no)	Logistic regression	Non-metropolitan women (versus metropolitan) more likely to have a MST but adjusted difference not statistically significant (p≥0.05); no statistically significant differences in AS rates by residential location after adjustment. ¹¹
Lai <i>et al</i> 2007 ⁷¹	WA	Data linkage	WA Data Linkage System	1995-1999	2,703, had BCS or MST	Unplanned hospital readmission ¹²	Survival model (multiple events/ subject)	Metropolitan women (versus non-metropolitan) 10% (p<0.05) lower unplanned readmission rates after adjustment. 13
Martin et al 2006 ⁶⁵	WA	Data linkage	WA Data Linkage System	1990-1999	2,713, one primary BC	BCS versus MST	Classificatio n trees, Logistic regression	Non-metropolitan women (versus metropolitan) significantly (p<0.001) more likely to choose MST after adjustment. ¹⁴
Mastaglia & Kristjanson 2001 ⁶⁶	WA	Cross-sectional	WA CR	1996-1997	160, Stage I-II	BCS versus MRM	Chi-square	Non-metropolitan women significantly (p<0.001) more likely to choose MRM than BCS (71% versus 36% metropolitan).
Mitchell et	WA	Cohort	WA CR	1999	899 (492 BCS,	BCS, adjuvant	Chi-square	Non-metropolitan women (versus metropolitan)

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Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
al 2006 ³⁶					692 HR+) histologically verified	RT, CT, HT, High (>=20 cases/year) caseload surgeon (all yes/no)		less likely to have BCS (42% versus 59%, p<0.001), RT (43% versus 55%, p=0.004), HT (64% versus 70%, if HR +, 75% versus 85%, p=0.003-0006) or high caseload surgical care (70% versus 86%, p<0.001); no statistically significant (p≥0.448) differences in post BCS- RT rates or CT.
Morris <i>et al</i> 2012 ⁷²	National	Audit	NBCA, NSW CCR, Vic CR, MBS	2008 (last 6 months)	1,334 (NBCA), 1,359 (NSW), 1,267 (Vic), ≤30mm size tumours	SNB (yes/no)	Two proportion z- tests (pooled)	Non-metropolitan women less likely to have a SNB among NCBA (66% versus 82% metropolitan), NSW (76% versus 86%) and Victorian (65% versus 81%) cohorts.
Ristevski et al 2012 ⁷⁹	Vic	Cross-sectional	Recruited by surgeons and nurses (one regional area)	NS	70, first primary early disease ⁵ , ≥six weeks postsurgery	Satisfaction, Referral (medical/ service type)	Descriptive, Fischer's exact test	97% of sample satisfied with treatment decision process regardless of surgical procedure. 42% referred to other health professionals/service before surgery.
Roder <i>et al</i> 2013a ⁴²	National	Non- representative sample	NBCA database ⁴	1998-2010	30,299, early disease ⁵ , residential postcodes noted	BCS versus MST, adjuvant RT, CT, Low (<=10 cases/year) caseload surgeon (all yes/no)	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) significantly less likely (p≤0.05) to have BCS (6%) or RT after BCS (7%) but more likely to have CT (10%), care at regional (4-31% versus major city) or remote centres (7 times) and low caseload care (9%, p=0.074) after adjustment. ¹⁵
Roder <i>et al</i> 2013b ²⁶	National	Non- representative sample	NBCA database ⁴	1998-2010	30,299, early disease ⁵ , residential postcodes noted	BCS versus MST, Low (<=10 cases/year) caseload surgeon (yes/no)	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) more likely to have MST (5-9 times, adjusted ¹⁶); and in bivariate analysis (p<0.001) low caseload surgical care or care outside major cities. Low surgical caseload significant (p<0.05) predictor of treatment outside major cities and higher MST.
Roder <i>et al</i> 2013c ⁷⁵	National	Non- representative sample	NBCA database ⁴	1998-2010	12,207, early disease ⁵ , prior MST, residential postcodes noted	IBR versus delayed or no BR after MST	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 13% less likely to have IBR (bivariate, p=0.043). Metropolitan rather than inner regional treatment centre and high (≥11 cases/year) surgical caseload significant (p<0.001) predictors of IBR after multivariate adjustment. 17
Roder <i>et al</i> 2012b ⁸⁷	National	Non- representative sample	NBCA database ⁴	1998-2005	36,775, early disease ⁵ , residential	Declining recommended treatment (yes/no)	Chi-square, Logistic regression	Percentage declining a treatment increased with remoteness of treatment centre (3% major cities, 5-9% outside major cities, p<0.001). Non-

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Results
					postcodes noted			metropolitan centres and low surgical caseload (≤20 cases/year) significant predictors of women declining BCS or RT (p<0.001); MST, AS or CT (caseload only, p≤0.003); HT (location, p<0.001). ¹⁸
Thompson et al 2008 ⁶⁷	Qld	Data linkage	Qld CR, Qld HAPDC	2004, 2004-2005 HAPDC record	1,274, early disease ⁵ , could be linked to medical records	MST, AS	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 2 times more likely to have MST, no statistically significant (p=0.196) differences in AS rates after adjustment. ¹⁹
Tulloh & Goldsworthy 1997 ⁸⁰	Vic	Medical chart reviews	Single rural centre	1992-1995	28 women	BCS versus MST	Descriptive	Rural setting no impediment to BCS (68%) or a multidisciplinary approach (93%).

AS axillary surgery (lymph nodes), BC Breast Cancer, BCN breast cancer nurse, BCS breast conservation surgery, BR breast reconstruction, BS BreastScreen, CR Cancer Registry, CCR Central Cancer Registry, CT chemotherapy, HAPDC Hospital Admitted Patient Data Collection, HR hormone receptor, HT hormone therapy, IBR immediate breast reconstruction, ISC Inpatient Statistics Collection, MBS Medical Benefits Schedule, MRM modified radical mastectomy, MST mastectomy, NBCA National Breast Cancer Audit, SBN specialist breast nurse, SE South-East, SNB sentinel node biopsy, RT adjuvant radiotherapy

- 1. National: all states/territories; ACT: Australian Capital Territory; NSW: New South Wales; Qld: Queensland: SA: South Australia; Vic: Victoria and WA Western Australia
- 2. Female invasive breast cancers cases
- 3. Adjusted for age at diagnosis, spread of disease, interaction between degree of spread and residential location.
- 4. National Breast Cancer Audit Database covers about 60% of early invasive female breast cancers diagnosed in Australia between 1998 and 2010.
- 5. Early disease defined as invasive tumours of ≤ 50mm diameter with either impalpable or palpable but not fixed lymph nodes and no evidence for distant metastases.
- 6. Adjusted for presence/absence of a radiotherapy facility in the same postcode as residential location of patient.
- 7. A final questionnaire completed up to 3 years post diagnosis.
- 8. Adjusted for age at diagnosis, socio-demographic factors and radiotherapy.
- 9. Adjusted for age at diagnosis, diagnostic period, Indigenous status, socio-demographic factors, comorbidities, area-disadvantage and hospital related factors.
- 10. Adjusted for age at diagnosis, diagnostic period, language spoken at home, clinical features, area-disadvantage, symptom status, cancer history and surgical caseload
- 11. Adjusted for age at diagnosis, area-disadvantage and country of birth.
- 12. Defined as within 42 days from initial surgery
- 13. Adjusted for age at diagnosis, clinical features, initial surgical procedure, health insurance status, country of birth and interactions between these variables.
- 14. Adjusted for age at diagnosis, clinical features, Indigenous status, socio-demographic factors and country of birth.
- 15. Adjusted for diagnostic period, area disadvantage and treatment centre location.
- 16. Adjusted for tumour size
- 17. Adjusted for age and year at diagnosis, clinical features, area-disadvantage, referral source, health insurance status, surgeon caseload and treatment-factors.
- 18. Adjusted for age at diagnosis, clinical features, treatment centre location, private health insurance status and surgeon caseload
- 19. Adjusted for age at diagnosis, tumour size, comorbidities, hospital type and surgical caseload.

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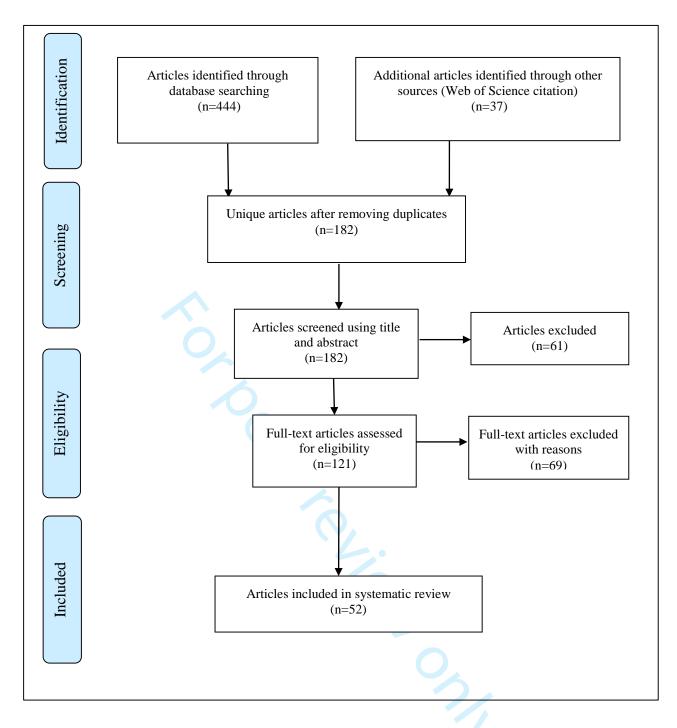
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Additional file 1 Database-specific search queries by individual clinical questions

Electronic databases searched: PubMed (1990- March Week 1, 2015), EMBASE (1990- March Week 1, 2015) and CINAHL (1994- March Week 1, 2015)

All search queries were conducted in a stepwise manner by breaking down each question into key concepts. Each numbered step in Tables below corresponds to the query used for an individual element such as Breast Cancer or Australia. For each element alternative terms were used to cover all possible synonyms for that component. Finally the individual search queries were combined to create the final search query using BOOLEAN operators such as "AND" or "OR".

1. In women diagnosed with breast cancer, do non-metropolitan women have poorer breast cancer survival compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	(((((((("survival"[MeSH Terms]) OR mortality[MeSH Terms]) OR "survival rate"[MeSH Terms]) OR "disease free survival"[MeSH Terms]) OR excess mortality[MeSH Terms]) OR survival analyses[MeSH Terms]) OR survival analyses[MeSH Terms]) OR cancer-specific survival[MeSH Terms]) OR event free survival[MeSH Terms]
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'survival'/exp OR 'survival' OR 'cancer mortality'/exp OR 'cancer mortality'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('survival'/exp OR 'survival' OR 'cancer mortality'/exp OR 'cancer mortality') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Survival") OR (MH "Survival Analysis+") OR (MH "Mortality+") OR TX 'survival'
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

2. In women diagnosed with breast cancer, do non-metropolitan women have different socio-demographic characteristics compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'demography'/exp OR 'demography' OR 'socioeconomics'/exp OR 'socioeconomics' OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health disparity' OR 'health care disparity'
#4	(age OR 'risk factor' OR 'lifestyle' OR 'health insurance' OR 'comorbidity') AND ('incidence'/exp OR 'incidence')
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'demography'/exp OR 'demography' OR 'socioeconomics'/exp OR OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health disparity' OR 'health disparity' OR 'health disparity' OR 'health disparity' OR 'health insurance' OR 'comorbidity') AND ('incidence'/exp OR 'incidence') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)

Search	Query
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural
	Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare
	Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Middle Age") OR (MH "Age Factors") OR (MH "Life Style+") OR (MH "Risk Factors+") OR (MH "Insurance, Health+") OR (MH "Insurance, Health+") OR (MH "Marital
	Status+") (MH "Demography+") OR (MH "Residence Characteristics+") OR (MH "Geographic Factors") OR (MH "Comorbidity") OR "comorbidities"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

3. In women diagnosed with breast cancer, do non-metropolitan women have more advanced tumour characteristics compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'cancer staging'/exp OR 'cancer staging' OR 'cancer grading' OR 'cancer size' OR 'metastasis'/exp OR 'metastasis'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('cancer staging'/exp OR 'cancer staging' OR 'cancer grading' OR 'cancer size' OR 'metastasis'/exp OR 'metastasis') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health Services") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MM "Neoplasm Staging") OR (MM "Neoplasms, Multiple Primary+") OR AB 'cancer grade' OR "cancer stage"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

4. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to access breast cancer screening services compared to metropolitan women in Australia?

PUBMED search query

Searc	h Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'mammography'/exp OR 'mammography' OR 'cancer screening'/exp)
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('mammography'/exp OR 'mammography' OR 'cancer screening'/exp) AND (rate* OR utiliz*) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mammography") OR (MH "Cancer Screening")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

5. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to adhere to recommended breast cancer screening intervals (2 yearly) compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

EMBASE search query (via EBSCO host)

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'
#4	'mammography'/exp OR 'mammography' OR 'cancer screening'/exp)
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('mammography'/exp/mj OR 'mammography' OR 'cancer screening'/exp) AND (rescreen* OR second* OR return*) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Health Services") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mammography") OR (MH "Cancer Screening")
S6	TX rescreen* OR TX "mammography second"
S7	S3 AND S4 AND S5 AND S6; English Language; Peer Reviewed; female

6. In women diagnosed with breast cancer, are there differences in clinical management between non-metropolitan and metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'clinical practice'/exp OR 'cancer adjuvant chemotherapy'/exp OR 'cancer chemotherapy'/exp OR 'cancer radiotherapy'/exp OR 'cancer hormonal therapy'/exp OR 'mastectomy'/exp OR 'mastectomy' OR 'lymph node dissection'/exp OR 'breast reconstruction'/exp OR 'breast reconstruction' OR 'cancer therapy multimodality'/exp
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('clinical practice'/exp OR 'cancer adjuvant chemotherapy'/exp OR 'cancer chemotherapy'/exp OR 'cancer radiotherapy'/exp OR 'cancer hormonal therapy'/exp OR 'mastectomy' OR 'mastectomy' OR 'lymph node dissection'/exp OR 'breast reconstruction'/exp OR 'breast reconstruction' OR 'cancer therapy multimodality'/exp) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mastectomy+") OR (MH "Lumpectomy") OR (MH "Chemotherapy, Cancer+") OR (MH "Chemotherapy, Adjuvant") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Cancer+") OR (MH "Breast Reconstruction") OR "Surgical patterns" or "case management"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

7. In women diagnosed with breast cancer, are non-metropolitan women less likely to receive the recommended clinical management compared to metropolitan women in Australia

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)

Search	Query
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'cancer adjuvant chemotherapy'/exp OR 'cancer adjuvant chemotherapy' OR 'cancer chemotherapy'/exp OR 'cancer chemotherapy' OR 'cancer combination chemotherapy'/exp OR 'cancer combination chemotherapy' OR 'cancer radiotherapy'/exp OR 'cancer radiotherapy' OR 'cancer hormonal therapy'/exp OR 'lymph node dissection'/exp OR 'lymph node dissection' OR 'cancer therapy'/exp OR 'sentinel node biopsy' OR 'cancer therapy multimodality'/exp OR 'cancer therapy multimodality'/exp OR 'cancer therapy multimodality'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('cancer adjuvant chemotherapy'/exp OR 'cancer adjuvant chemotherapy' OR 'cancer chemotherapy'/exp OR 'cancer chemotherapy'/exp OR 'cancer combination chemotherapy' OR 'cancer radiotherapy'/exp OR 'cancer radiotherapy' OR 'cancer radiotherapy' OR 'cancer therapy'/exp OR 'cancer therapy'/exp OR 'sentinel node biopsy' OR 'cancer therapy multimodality'/exp OR 'cance

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"

Search	Query
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Chemotherapy, Cancer+") OR (MH "Chemotherapy, Adjuvant") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Adjuvant") OR (MH "Combined Modality Therapy+") OR (MH "Breast Reconstruction")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

8. In women diagnosed with breast cancer, are non-metropolitan women more likely to experience delays in referral to breast cancer specialist clinicians compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology)))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'referral and consultation'/exp OR 'referral and consultation' OR 'public hospitals' OR 'private hospitals' OR (surgical AND caseload) OR 'hospital volume' OR 'surgical volume'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('referral and consultation'/exp OR 'referral and consultation' OR 'public hospitals' OR 'private hospitals' OR (surgical AND caseload) OR 'hospital volume' OR 'surgical volume') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH " Referral and Consultation+")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

9. In women diagnosed with breast cancer, do non-metropolitan women experience fewer treatment options compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

EMBASE	MBASE search query (via EBSCO host)	
Search	Query	
#1	'breast cancer'/exp OR 'breast cancer'	
#2	'australia'/exp	
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR	
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'	
#4	'patient decision making'/exp OR 'patient decision making' OR 'patient decision aid' OR 'patient delay'	
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural	
	difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care	
	disparity'/exp OR 'health care disparity') AND 'patient decision making'/exp OR 'patient decision making' OR 'patient decision aid' OR 'patient delay' AND [english]/lim AND	
	[female]/lim AND [1990-2015]/py	

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Decision Making, Patient+")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

10. In women diagnosed with breast cancer, are non-metropolitan women less likely to complete prescribed treatment compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) ((((((((((((((((((((((((((((((((

EMBASE search query (via EBSCO host)

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'patient compliance'/exp OR 'patient compliance' OR 'treatment refusal'/exp OR 'treatment refusal'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('patient compliance'/exp OR 'patient compliance' OR 'treatment refusal'/exp OR 'treatment refusal') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Patient Compliance+") OR (MH "Treatment Refusal")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

11. In women diagnosed with breast cancer, are non-metropolitan women less likely to participate in recommended follow-up compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query			
#1	breast cancer'/exp OR 'breast cancer'			
#2	'australia'/exp			
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR			
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'			
#4	'postoperative care'/exp OR 'postoperative care' OR 'patient care'/exp OR 'patient care' OR 'survivorship' OR 'survivorship care plan'			
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp/mj AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('postoperative care'/exp OR 'postoperative care' OR 'patient care'/exp OR 'patient care' OR 'survivorship' OR 'survivorship care plan') AND [english]/lim AND [female]/lim AND [humans]/lim			

CINAHL search query (via EBSCO host)

Search	Query		
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"		
S2	(MH "Australia+")		
S3	(S1 AND S2)		
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural		
S5	(MH "Postoperative Care+") OR (MH "Patient Care+") OR (MH "After Care")		
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female		

Additional searches:

We also searched the INFORMIT database (1994- March Week 1, 2015)

Informit Health (Australian databases) search query

Search	Query			
#1	(Breast Cancer) OR (Breast Neoplasm)			
#2	MH: Australia			
#3	(MH:Australia) AND ((Breast Cancer) OR (Breast Neoplasm))			
#4	((MH:Australia) AND ((Breast Cancer) OR (Breast Neoplasm))) AND ((ALLTERMS:rural OR geography OR (rural health) OR socioeconomic OR inequalities))			

Additional file 2: Quality appraisal tools for included quantitative studies

I. Selection bias (Sample selection for cohort studies)	Score		
Representative of population of interest	2		
Selected group, somewhat representative			
Highly selected, convenient or not described			
II. Assessment (or measurement) of exposure and or confounding variables			
Secure records, independent blind assessment	2		
Independent assessment un-blinded; self-reported	1		
No description or unclear how exposure was assessed	0		
III. Assessment (or measurement) of outcome			
Record linkage, independent blind assessment, previously validated/reliable measures	2		
Independent assessment un-blinded; self-report, novel measures (validation/ reliability data provided	1		
Novel measures (no validation/reliability tests) or assessment of outcome not described	0		
IV. Adequacy of follow-up and/or were all patients included			
Yes (follow-up > 95%) of patients or > 95% of all patients included	2		
Reasonable follow-up of all patients or all patients included (>80%)	1		
\leq 80% of patients /included patients followed-up, not described or not relevant	0		
V. Adequacy of adjustment for confounding: (matching, stratification, multivariate analysis			
Yes	2		
Not clear or not applicable	1		
No	0		
VI. If there was adjustment for residual confounding			
Study comprehensively controls for age and additional risk factors	2		
Study controls for age and most plausible additional factors			
Minimum matching or adjustment for plausible prognostic variables; no adjustment			
VII. Attrition (missing data): If a concern was missing data handled appropriately			
Yes	2		
Not clear or not applicable	1		
No	0		
VIII. Statistical methods adequate or appropriate and sufficiently described			
Yes	2		
Not clear or not applicable	1		
No	0		
IX. Data presentation			
Examples of data presented allows clear understanding of data analysis and interpretation	2		
Examples provided but do not present a clear interpretation of data			
Very little data presented or incomplete recording			

Additional file 3: Excluded studies with reasons for exclusion

Study Reference	Reason for Exclusion
Achat et al 2005 ¹	No results by residential location of women or for rural women
Andreeva & Pokhrel 2013 ²	Does not assess one of the considered clinical questions
Azzopardi <i>et al</i> 2014 ³	No results by residential location of women or for rural women
Banks <i>et al</i> 2010 ⁴	No results specifically for female breast cancer patients
Banks <i>et al</i> 2014 ⁵	No results specifically for female breast cancer patients
	No results by residential location or for rural women in target
Barratt et al 1999 ⁶	screening age group
Beckmann <i>et al</i> 2011 ⁷	Does not assess one of the considered clinical questions
Bell <i>et al</i> 2009 ⁸	Does not assess one of the considered clinical questions
Bessen et al 2014 ⁹	Does not assess one of the considered clinical questions
Bessen & Karnon 2014 ¹⁰	Does not assess one of the considered clinical questions
Boyages et al 2010 ¹¹	Does not assess one of the considered clinical questions
Brennan & Spillane 2013 ¹²	Review
Brennan & Houssami 2006 ¹³	Does not assess one of the considered clinical questions
Brennan <i>et al</i> 2014 ¹⁴	Review
Brennan et al 2010 ¹⁵	Survey of health professionals rather than women with breast cancer
Brennan <i>et al</i> 2010 ¹⁶	Does not assess one of the considered clinical questions
Brennan <i>et al</i> 2011 ¹⁷	Does not assess one of the considered clinical questions
Brennan <i>et al</i> 2011 ¹⁸	Opinion piece
2. 2	No results by residential location or for rural women in target
Brown <i>et al</i> 2013 ¹⁹	screening age group
Buckley et al 2014 ²⁰	Does not assess one of the considered clinical questions
Budden et al 2007 ²¹	Does not assess one of the considered clinical questions
Budden et al 2003 ²²	Does not assess one of the considered clinical questions
Butler-Henderson et al 2014 ²³	In situ and not invasive breast cancer
Canfell 2014 ²⁴	Review
Carrick <i>et al</i> 1998 ²⁵	Opinion piece
Chavez-Macgregor & Hortobagyi 2011 ²⁶	Opinion piece
Chin <i>et al</i> 2008 ²⁷	In situ and not invasive breast cancer
Chisholm et al 2000 ²⁸	Does not assess one of the considered clinical questions
	Economic analysis: Does not assess one of the considered clinical
Clarke 1998 ²⁹	questions
GL 1 2002 ²⁰	Economic analysis; Does not assess one of the considered clinical
Clarke 2002 ³⁰	questions
Clover <i>et al</i> 1996 ³¹	No results by residential location or for rural women in target screening age group
C10 vC1 e1 u1 1770	No results by residential location or for rural women in target
Cockburn et al 1991 ³²	screening age group
	No results by residential location or for rural women in target
Cockburn et al 1997 ³³	screening age group
Coleman et al 2011 ³⁴	A comparative study across countries only
Coleman et al 2008 ³⁵	A comparative study across countries only
	No information by patient's residential location; only by treatment
Craft <i>et al</i> 2010 ³⁶	centre location
Cramb <i>et al</i> 2012 ³⁷	Does not assess one of the considered clinical questions
Cramb <i>et al</i> 2011 ³⁸	No results specifically for female breast cancer patients
Crombie et al 2005 ³⁹	No results by residential location of women or for rural women
Davey <i>et al</i> 2008 ⁴⁰	Does not assess one of the considered clinical questions
Delpizzo 1995 ⁴¹	Does not assess one of the considered clinical questions
Dowling et al 2014 ⁴²	Does not assess one of the considered clinical questions

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-	Study Reference	Reason for Exclusion
-	Emery 2010 ⁴³	Conference abstract
	Emery <i>et al</i> 2013 ⁴⁴	No results specifically for female breast cancer patients
	Fisher <i>et al</i> 2014 ⁴⁵	Not Australian-based
	Fong <i>et al</i> 2012 ⁴⁶	A comparative study across countries only
	Fong <i>et al</i> 2012 ⁴⁷	A comparative study across countries only
	Frensham et al 2014 ⁴⁸	No results specifically for female breast cancer patients
	Furnival 2004 ⁴⁹	Editorial
	Furnival 1997 ⁵⁰	Editorial
	Giles <i>et al</i> 2010 ⁵¹	Methodological paper
	Goldsbury et al 2012 ⁵²	Not breast cancer
	Green <i>et al</i> 2013 ⁵³	Conference abstract
	Halkett <i>et al</i> 2014 ⁵⁴	Study protocol
	Halkett <i>et al</i> 2006 ⁵⁵	No results by residential location of women or for rural women
	Harden <i>et al</i> 2014 ⁵⁶	Conference abstract
	Harrison <i>et al</i> 2008 ⁵⁷	No results by residential location of women or for rural women
	Hayes <i>et al</i> 2010 ⁵⁸	No results by residential location of women or for rural women
	Heathcote & Armstrong 2007 ⁵⁹	Review
	Hersch et al 2014 ⁶⁰	Study protocol
	Heywood <i>et al</i> 1994 ⁶¹	Does not assess one of the considered clinical questions
	Hunt et al 2001 ⁶²	Does not assess one of the considered clinical questions
	Hyndman & Holman 2000 ⁶³	Does not assess one of the considered clinical questions
	Hyndman et al 1997 ⁶⁴	Does not assess one of the considered clinical questions
	Tryndinan et at 1997	No information by patient's residential location; only by surgical
	Ingram <i>et al</i> 2005 ⁶⁵	caseload
	Jones 2004 ⁶⁶	Opinion piece
	Jong et al 2005 ⁶⁷	Opinion piece
	Kavanagh et al 1999 ⁶⁸	Does not assess one of the considered clinical questions
	Kiely <i>et al</i> 2013 ⁶⁹	Does not assess one of the considered clinical questions
	·	Includes women with high breast cancer risk, no results by residential
	Kiely <i>et al</i> 2010 ⁷⁰	location
	Kremser et al 2008 ⁷¹	Does not assess one of the considered clinical questions
	Kricker 1998 ⁷²	Review
	Kricker et al 2008 ⁷³	Does not assess one of the considered clinical questions
	Kricker et al 2009 ⁷⁴	No results by residential location of women or for rural women
	Kwok & White 2011 ⁷⁵	Does not assess one of the considered clinical questions
	Lawler et al 2012 ⁷⁶	Does not assess one of the considered clinical questions
	Llewellyn et al 2011 ⁷⁷	Does not assess one of the considered clinical questions
	70	Includes women with high breast cancer risk, no results by residential
	Lobb <i>et al</i> 2002 ⁷⁸	location
	Lopez <i>et al</i> 2013 ⁷⁹	Not breast cancer
	Lu et al 2013 ⁸⁰	Does not assess one of the considered clinical questions
	Luke <i>et al</i> 2006 ⁸¹	Does not assess one of the considered clinical questions
	Luke <i>et al</i> 2003 ⁸²	No results specifically for female breast cancer patients
	Magiros et al 2001 ⁸³	Does not assess one of the considered clinical questions
	14. 1 1200084	No information by patient's residential location; only by treatment
	Marsh <i>et al</i> 2008 ⁸⁴	centre location
	Mauad <i>et al</i> 2009 ⁸⁵	Not Australian-based
	McCredie <i>et al</i> 1995 ⁸⁶	Review
	McMichael <i>et al</i> 2000 ⁸⁷	Does not assess one of the considered clinical questions
	Moorin & Holman 2006 ⁸⁸	Does not assess one of the considered clinical questions
_	Moran & Warren-Forward 2011 ⁸⁹	Does not assess one of the considered clinical questions

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_	Study Reference	Reason for Exclusion		
_	Morley et al 2010 ⁹⁰	Only included women from urban areas		
	Morrell et al 2012 ⁹¹	Does not assess one of the considered clinical questions		
	Ogunsiji et al 2013 ⁹²	Does not assess one of the considered clinical questions		
	Paddison &Yip 2010 ⁹³	Not breast cancer		
	Page et al 2006 ⁹⁴	Does not assess one of the considered clinical questions		
	Peters 2012 ⁹⁵	Does not assess one of the considered clinical questions		
	Protani et al 2012 ⁹⁶	Does not assess one of the considered clinical questions		
	Richardson 2013 ⁹⁷	Opinion piece		
	Roder <i>et al</i> 2011 ⁹⁸	Conference abstract		
	Rychetnik et al 2013 ⁹⁹	Editorial		
	Sandelin et al 2003 ¹⁰⁰	Does not assess one of the considered clinical questions		
	Sharplin et al 2014 ¹⁰¹	No results specifically for female breast cancer patients		
	Shugg et al 2002 ¹⁰²	Ductal carcinoma and not invasive breast cancer		
	Smith 2012 ¹⁰³	Review		
		No information by patient's residential location; only by treatment		
	Somogyi <i>et al</i> 2015 ¹⁰⁴	centre location		
	Speedy & Hase 2000 ¹⁰⁵	Does not assess one of the considered clinical questions		
		No outcomes by patient's residential location; only by treatment centre		
	Spillane <i>et al</i> 1999 ¹⁰⁶	location		
	Spillane <i>et al</i> 2001 ¹⁰⁷	No results by residential location of women or for rural women		
	Spilsbury et al 2005 ¹⁰⁸	Does not assess one of the considered clinical questions		
	Stanton <i>et al</i> 1995 ¹⁰⁹	Does not assess one of the considered clinical questions		
	Sullivan et al 2004 ¹¹⁰	Does not assess one of the considered clinical questions		
	Taylor <i>et al</i> 1999 ¹¹¹	Only included women from urban areas		
	Taylor <i>et al</i> 2003 ¹¹²	No results by residential location of women or for rural women		
	Thewes et al 2003 ¹¹³	Review		
	Thiruvarudchelvan et al 2010 ¹¹⁴	Does not assess one of the considered clinical questions		
	Turnbull <i>et al</i> 1994 ¹¹⁵	Does not assess one of the considered clinical questions		
	Villanueva et al 2008 ¹¹⁶	No results by residential location of women or for rural women		
	Ward et al 2000 ¹¹⁷	Does not assess one of the considered clinical questions		
	Weller 1998 ¹¹⁸	Not breast cancer		
		No information by patient's residential location; only by treatment		
	Whitfield et al 2012 ¹¹⁹	centre location		
	Wilcoxon <i>et al</i> 2011 ¹²⁰	No results specifically for female breast cancer patients		
	Willis 2004 ¹²¹	Looks at women outside the target age group for screening		
	Willis & Baxter 2003 ¹²²	Looks at women outside the target age group for screening		
	Winefield et al 2004 ¹²³	Does not assess one of the considered clinical questions		
	Wong et al 2014 ¹²⁴	No results by residential location of women or for rural women		
	Woods et al 2010 ¹²⁵	A comparative study across countries only		
	Yelland et al 1991 ¹²⁶	No results by residential location of women or for rural women		
	Youl et al 2011 ¹²⁷	Study protocol		
	Yu et al 2006 ¹²⁸	Does not assess one of the considered clinical questions		
	Zardawi <i>et al</i> 1999 ¹²⁹	Does not assess one of the considered clinical questions		
	Zilliacus et al 2010 ¹³⁰	Genetic counselling		

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #		
TITLE					
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1		
ABSTRACT					
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2		
INTRODUCTION					
Rationale	3	Describe the rationale for the review in the context of what is already known.	4		
8 Objectives 9	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5, Table 1		
METHODS					
2 Protocol and registration 3	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NR		
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6		
7 Information sources 8	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5		
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file 1		
2 Study selection 3	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7		
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7		
7 Data items 8	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	NR		
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6		
2 Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NR		
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., 12) for each meta-analysis com/site/about/guidelines.xhtml	7		



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PRISMA 2009 Checklist

Page 1 of 2					
Section/topic	#	Checklist item	Reported on page #		
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6		
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NR		
RESULTS					
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, Figure 1		
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Tables 2-		
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7-8, Tables 2- 6		
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-12, Tables 2- 6		
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NR		
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NR		
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NR		
DISCUSSION					
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-13		
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14		
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15		
FUNDING					
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	16		

45 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097.



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doi:10.1371/journal.pmed1000097



BMJ Open

Variations in outcomes by residential location for women with breast cancer: a systematic review

Journal:	BMJ Open		
Manuscript ID	bmjopen-2017-019050.R1		
Article Type:	Research		
Date Submitted by the Author:	14-Dec-2017		
Complete List of Authors:	Dasgupta, Paramita; Cancer Council Queensland, Cancer Research Centre Baade, Peter; Cancer Council Queensland, Cancer Research Centre Youlden, Danny; Cancer Council Queensland, Cancer Research Centre Garvey, Gail; Menzies School of Health Research, Epidemiology and Health Systems Aitken, Joanne; Cancer Council Queensland, Cancer Research Centre Wallington, Isabella; Cancer Australia Chynoweth, Jennifer; Cancer Australia Zorbas, Helen; Cancer Australia Youl, Philippa; Cancer Council Queensland, Cancer Research Centre		
Primary Subject Heading :	Epidemiology		
Secondary Subject Heading:	Oncology		
Keywords:	Breast tumours < ONCOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH		
	SCHOLARONE™ Manuscripts		

Variations in outcomes by residential location for women with breast cancer: a systematic review

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Word length:

Manuscript word count (excluding title page, abstract, references, figure legends, and tables): 4964

Abstract word count: 287

References: 142

Tables: 6

Figures: 1

Supplementary files: 4

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Abstract

Objectives: To systematically assess the evidence for variations in outcomes at each step along the breast cancer continuum of care for Australian women by residential location.

Design: Systematic review

Methods: Systematic searches of peer-reviewed articles in English published from 1/1/1990 to 24/11/2017 using PubMed, EMBASE, CINAHL and Informit databases. Inclusion criteria were: population was adult female breast cancer patients; Australian setting; outcome measure was survival, patient or tumour characteristics, screening rates or frequencies, clinical management, patterns of initial care or post-treatment follow-up with analysis by residential location, or studies involving non-metropolitan women only. Included studies were critically appraised using a modified Newcastle-Ottawa Scale.

Results: Seventy-four quantitative studies met the inclusion criteria. Around 59% were considered high quality, 34% moderate and 7% low. No eligible studies examining treatment choices or post-treatment follow-up were identified. Non-metropolitan women consistently had poorer survival, with most of this differential being attributed to more advanced disease at diagnosis, treatment-related factors and socioeconomic disadvantage. Compared to metropolitan women, non-metropolitan women were more likely to live in disadvantaged areas and had differing clinical management and patterns of care. However, findings regarding geographical variations in tumour characteristics or diagnostic outcomes were inconsistent

Conclusions: A general pattern of poorer survival and variations in clinical management for Australian female breast cancer patients from non-metropolitan areas was evident. However, the wide variability in data sources, measures, study quality, time periods and geographical classification made direct comparisons across studies challenging. The review highlighted the need to promote standardization of geographical classifications and increased comparability of data systems. It also identified key gaps in the existing literature including a lack of studies on advanced breast cancer, geographical variations in treatment choices from the perspective of patients and post-treatment follow-up.

Keywords: Breast cancer; Non-metropolitan; Systematic review; Geographical variations; Continuum of care

Strengths and Limitations:

Strengths:

- First systematic review examining evidence for geographical variations in breast cancer outcomes across the continuum of care for Australian women
- Review was conducted according to published guidelines
- All included articles were subject to quality assessment

Limitations:

 Wide heterogeneity across studies in study quality, levels of evidence, methodology, data sources, time period and terminology

No meta-analysis was possible



Introduction

Worldwide, breast cancer is the most frequently diagnosed cancer among females, accounting for 25% of all new diagnoses in 2012 and is the leading cause of female cancer mortality (15% of total cancer deaths). Among Australian women, breast cancer is also the most common cancer and the second leading cause of cancer mortality. Like other developed countries, Australia has high breast cancer incidence rates but relatively low mortality rates with significant and ongoing improvements in survival, most likely due to earlier detection, screening mammography and improved treatments. However not all women have benefitted equally from these improvements with international studies consistently reporting geographical variations in survival and across the breast cancer continuum of care (such as screening, diagnosis, treatment, post-treatment and psychosocial care). While Australia has relatively high survival rates compared to international benchmarks, significant variations exist with poorer survival for rural and disadvantaged women.

Australia has a universal health-care system, however it is also a country of vast distances with cancer-related services typically being concentrated in major cities¹³ so that those living elsewhere often face long travel times and limited access to specialized care.^{11 14} Although about 20% of the total Australian population live outside a major city, for some states and territories this percentage increases to over a third.¹⁵ There is also considerable overlap between remoteness and socioeconomic status; around a third of the population living in major cities in Australia also live in areas classified as least disadvantaged, compared to only 2% of those from very remote areas.¹⁶ Current strategies to better address the needs of rural cancer patients and to make cancer care more accessible include the Australian Government's establishment of cancer centres and radiation facilities in regional Australia, exploring innovative models of care and other local-level initiatives.^{14 17}

A comprehensive understanding of the drivers of variations in outcomes across population groups is a prerequisite for ensuring equitable cancer care and improving outcomes for all Australians. This systematic review aimed to identify, assess and synthesize the current evidence relating to geographical variations in survival, patient and tumor characteristics, diagnostic and clinical outcomes for female Australian breast cancer patients. It was conducted as part of a larger systematic review that also investigated psycho-social outcomes¹⁸ and variations by Indigenous status.¹⁹ Such a review may help identify gaps in knowledge, formulate strategic research priorities and develop evidence-based interventions to reduce the observed inequities.

Methods

Terminology

Due to the range of definitions used to define geographical areas, geographical remoteness was categorised into "metropolitan" areas (typically "major cities" or "urban") and "non-metropolitan" areas (comprising the remaining localities). However, where relevant, important patterns observed within the remoteness categories were described in greater detail such as studies relating specifically to remote or very remote areas.

Clinical Questions

The published PRISMA guidelines for conducting systematic reviews²⁰ were followed for this review. As a first step, a series of clinical questions to guide the review were clearly defined and agreed upon before commencing the review process in consultation with a Project Steering Group that included clinicians, researchers, allied health practitioners, consumer advocates with experience in breast cancer and health policy representatives. All questions conformed to PICO guidelines²⁰ in which the target population (P), intervention/exposure (I), comparator (C) and outcomes (O) are clearly defined and used to guide the review process, with the comparator being the only optional component.²¹

Eleven clinical questions examining variations between non-metropolitan and metropolitan women with breast cancer (collectively referred to as 'residential location') were grouped according to 1) survival (one question); 2) patient/tumour characteristics (two questions); and 3) diagnostic and treatment outcomes (eight questions) (Table 1).

Literature searches

The electronic databases: PubMed, EMBASE, CINAHL and Informit were systematically searched for all indexed articles from 1 January 1990 to 24 November 2017. The Web of Science database was used for cited reference searches.

Search strategies were based on keywords and subject headings to reflect the review aim with separate queries designed for each clinical question (see Supplementary Appendix 1). Key terms of 'breast neoplasms', 'female' and 'Australia' were combined with terms relating to geographical aspects including 'rural health', 'geographic inequalities', 'spatial', 'health services accessibility' and 'remoteness' and outcome measures of interest notably 'survival', 'stage', 'diagnosis age', 'socioeconomic', 'mammography', 'screening rate', 're-screening'', 'clinical management', 'patterns of care', 'mastectomy', 'breast reconstruction', 'chemotherapy', 'radiotherapy', 'lymph node' and 'guideline adherence'. Additional synonyms reflecting each of the key terms were also included.

Inclusion criteria

Studies were eligible if they met the following inclusion criteria:

- 1) the population included adult female breast cancer patients or focussed on a breast cancer specific sub-group; and
- 2) had an Australian setting; and
- 3) the outcome measure was survival, patient or tumour characteristics, screening participation or frequency, clinical management, patterns of initial care or post-treatment follow-up; and
- 4) was
 - a) a quantitative study on non-metropolitan versus metropolitan comparisons; or
 - b) a qualitative study on geographical inequalities; or
 - c) quantitative or qualitative studies reporting on relevant outcomes for non-metropolitan women only.

The scope of the review was limited to English language peer-reviewed original research articles. Reviews, editorials, books, conference abstracts and commentaries were excluded, although when identified through the systematic searches their reference lists were examined for relevant articles.

Review process

After removing duplicates, the titles and abstracts of all articles identified during the searches were independently reviewed by two authors (first PD, second PY, DY or PB) for possible inclusion based on their relevance to each clinical question. Discrepancies were clarified through discussion between the two reviewers and if necessary the other reviewers were consulted. Full text versions of all articles of potential relevance were then retrieved for more detailed independent assessment by two reviewers as before. During this process articles were classified as "include" or "exclude" with reasons for exclusion being documented. Reviewer decisions were compared and any disagreements resolved by consensus.

Critical appraisal

The quality of all included articles was critically assessed by two independent reviewers using the Newcastle-Ottawa Scale (NOS),²² a risk of bias assessment tool for non-randomised studies recommended by the Cochrane Collaboration²³ that can be readily tailored for the critical appraisal of quantitative cohort studies.⁹ The NOS assesses studies on six items over five broad perspectives: (a) selection bias; (b) measurement of confounders; (c) outcome assessment; (d) follow-up and (e) adjustments for residual confounders (two items). We extended this tool by incorporating features from other published checklists²⁴ ²⁵ to include three additional items to assess (a) study attrition (missing data), (b) statistical methods and (c) data presentation. Studies were scored according to the extent that they met each of the nine assessed criterion (see Supplementary Appendix 2) using an ordinal scale to rate the risk of bias as 0 (high), 1 (intermediate) and 2 (low) and the individual item scores then summed to give a total quality score. Instances of major differences in total scores 6

between the two reviewers for individual articles were resolved by consensus and each article was then assigned a summary score (averaged across the two scores). The total average score (range of 0-18) achieved across the nine criterion was categorized as "high" (14-18), "moderate" (9-13.5) or "low" (<9) quality. Studies were not excluded based specifically on their quality rating.

Studies were also classified according to the published levels of evidence for quantitative observational studies from the Australian National Health and Medical Research Council (NHMRC)²⁴ in decreasing order of strength as Level I, Level II, Level III-1, Level III-2, Level III-3 or Level IV.

Data extraction

For all included articles, study characteristics including author(s), publication year, title, population, design and outcomes were recorded in a customized database by one reviewer and subsequently checked by another. Any errors or inconsistencies were resolved after consulting the original source.

Results

Study selection

The steps in the review process are illustrated in a PRISMA diagram (Figure 1). A total of 476 articles were identified across combined databases with an additional 45 citations from other sources. After removing duplicates, an initial pool of 211 articles remained of which 65 were excluded after initial scanning of title/abstracts. Of the 146 retrieved full-text articles, 74 met the inclusion criteria and were considered relevant to at least one of the clinical questions. Excluded studies are listed in Supplementary Appendix 3, including reasons for exclusion.

Study characteristics

All included articles were quantitative and around 80% used administrative data sources such as population-based cancer registries, screening databases or the non-representative (not population based) National Breast Cancer Audit database which has collected data on about 60% of invasive early breast cancers treated by participating Australian (and New Zealand) breast surgeons since 1998. Remaining studies were based on medical record reviews and cross-sectional surveys.

There was considerable heterogeneity in the definition of non-metropolitan and metropolitan populations. While more than half (57%) of the included studies used standardized definitions such as the Rural, Remote and Metropolitan Areas (RRMA) system, the Accessibility/Remoteness Index of Australia (ARIA) or ARIA+, or remoteness areas defined by the Australian Standard Geographical Classification,²⁷ others defined non-metropolitan and metropolitan areas based on distances to services, population density or postcodes. Two studies did not provide detailed information regarding the basis of their geographical classification (Table 2).

Around 59% of included studies were graded as high quality, 34% moderate and 7% low quality, with a mean score of 13.0 and range of 6.5-17.0. Key limiting factors for these scores were that around a third (30%) of studies did not use a population-based representative sample, while 20% did not adjust for confounders (including age and socio-demographics). Studies based on reliable and objective data sources (cancer registries) were limited in their ability to control for clinical and treatment factors. The use of highly selective or convenience samples and lack of follow-up also reduced study quality. No studies provided Level I evidence, while more than half (57%) gave Level II evidence, 34% Level III-3 and 9% Level-IV evidence (Table 2).

Key findings

Studies are summarized below (Tables 3-6, also Supplementary Appendix 4) according to clinical questions within each of the key themes: 1) survival outcomes, 2) patient/tumour characteristics and 3) diagnostic and treatment outcomes. Several studies reported on multiple outcomes. The emphasis is on whether there was evidence of variations in relevant outcomes by residential location and, if so, the direction and a quantitative estimate of the magnitude of the effect. Given the considerable heterogeneity among studies in terms of their quality, levels of evidence, time period and geographical definitions, we have deliberately interpreted any summary patterns with caution.

Survival Outcomes

There was a consistent pattern of significantly poorer survival (in unadjusted analyses) for women in non-metropolitan areas compared to metropolitan women across 21 (19 high and two moderate quality) of 22 included studies both nationally^{28 29} and at the state-level (Table 3).³⁰⁻⁴⁶ The five-year unadjusted relative survival for female breast cancers was about 2-5% (absolute) lower for non-metropolitan than metropolitan women. The one exception was an early high quality study involving women in New South Wales (diagnosed from 1980-1991) that did not report any survival differential.⁴⁷

However, no geographical differential in survival was evident across $11^{29\,33\,37\,38\,40-44\,47\,48}$ of 20 studies that also reported survival estimates after adjustment for various combinations of known survival determinants including demographics, area-level disadvantage, spread of disease, comorbidities and treatment-related factors. The remaining nine studies 30-32 34-36 39 45 49 all reported poorer survival for non-metropolitan women even after adjustment.

The adjusted results varied according to the combination of variables included in the statistical models. Six of the seven papers that reported significant differentials after adjusting for a measure of stage at diagnosis did not consider comorbidities or treatment-related factors. ^{30 31 34 35 39 45} Of the five studies that adjusted for treatment-related factors, four reported no evidence of a survival differential ³⁸

⁴⁰⁻⁴² while the finding of a significant difference was likely to be limited to women diagnosed prior to the mid-1990s in the remaining study.³²

Most of the 22 included studies focussed on medium-term survival, with only one⁴⁴ following women for longer than five years after their breast cancer diagnosis.

Patient and Tumour Characteristics

Patient characteristics

Both of the included high quality studies that reported a positive association between areadisadvantage and non-metropolitan residence were based on analysis of 30,299 early invasive female breast cancer cases from the National Breast Cancer Audit (Table 4).^{50 51} For example, compared to affluent women, socio-economically disadvantaged women diagnosed with breast cancer were 17 times more likely to live in remote areas (than metropolitan areas)⁵⁰ while compared to metropolitan women, those from remote areas were 13 times more likely to live in a disadvantaged rather than more advantaged region.⁵¹

Tumour characteristics

No consistent pattern of variations in tumour characteristics by residential location were evident across the 13 included studies (Table 4). Nationally, one high quality study found that non-metropolitan women were 15% more likely to present with tumours >40mm (versus <30mm)²⁶ while three state-based high quality studies also reported similar patterns, ⁵²⁻⁵⁴ despite using different definitions of advanced disease. However, eight others (four high, four moderate quality) showed no differences^{30 40 46 55-59} and one (high quality) that metropolitan women were 11% more likely to present with regional disease than non-metropolitan patients, but equally likely to present with distant tumours.⁴⁴

Diagnostic and Treatment Outcomes

Studies described here assessed geographical variations in relation to two broad topics: breast cancer screening (Table 5) and treatment (Table 6). The target group for the two screening questions refers to women aged 50 to 69 who were eligible (at the time of this review) for the free population-based national mammographic program in Australia (BreastScreen Australia).⁶⁰

Screening rate

All eight of the included moderate quality studies relate to the publicly funded BreastScreen program, as there were no data available to assess variations in private mammography, and provided mixed results. Analyses of self-reported data for more than 10,000 women nationally found that despite poorer access to mammography services, ⁶¹ non-metropolitan women had similar screening rates to 9

metropolitan women, ^{61 62} consistent with an earlier cross sectional survey. ⁶³ Two state-based studies however reported higher participation rates in the BreastScreen program for non-metropolitan women. ^{64 65} In contrast women who lived within 10-20 km of a relocatable BreastScreen service were 43% less likely to have been screened than those residing within 2 km of the service. ⁶⁶ Another study found that non-metropolitan women in the target age group were 39% more likely to report never having been screened through through BreastScreen Australia than metropolitan women. ⁶⁷ Screening history, perceived breast cancer risk and knowledge about service location were among key predictors of accessing a relocatable screening service in a study involving only 180 non-metropolitan women. ⁶⁸

Rescreening

Results were inconsistent across the five included studies, with a dependence on the time period of data collection. One early (moderate quality) study showed that metropolitan women had higher rescreening rates through the national BreastScreen program than non-metropolitan women⁶⁷ whereas among four other studies from 1995 onwards, one (moderate quality) study showed no difference in rescreening rates⁶⁹ and three studies (two moderate, one high quality) showed that non-metropolitan women had higher rescreening rates.^{61 70}

Clinical management

Given there are separate Australian guidelines for clinical management of early⁷¹ and advanced stage breast cancer,⁷² the descriptions of variations in clinical management are categorised accordingly.

A consistent pattern of variations in the clinical management of early breast cancer by residential location was evident across 21 (14 high, six moderate, one low quality) of 28 included studies with seven (three high, two moderate, two low) finding no variations.

Among 30,299 cases extracted from the National Breast Cancer Audit database, non-metropolitan women were at least five times more likely to have a mastectomy than metropolitan women²⁶ while another study using this database reported that the proportion of mastectomies progressively increased with increasing remoteness.⁷³ Various state-specific studies also reported similar patterns.⁷⁴⁻⁷⁷ Studies using the National Breast Cancer Audit database found that non-metropolitan women were 6% less likely to undergo breast conserving surgery⁵⁰ and that the proportion who had breast conserving surgery decreased progressively with increasing remoteness.⁷³ Similar findings were evident across six other state-level studies. ^{40 54 74 78-80} Only three studies reported no differences in surgical patterns by residential location. ⁸¹⁻⁸³

Two studies based on the National Breast Cancer Audit Database reported that non-metropolitan women were up to 20% less likely to receive adjuvant radiotherapy than metropolitan women. ^{50 73} Moreover women residing in areas lacking radiotherapy facilities had a higher likelihood (23%) of not

receiving radiotherapy than those from regions with such facilities.⁷³ Three state-based studies also reported similar patterns.^{40 54 84} Findings for other treatment modalites were less consistent with no geographical differentials in receipt of either hormonal therapy^{84 85} or chemotherapy,^{40 80 84} higher uptake of chemotherapy⁵⁰ and lower for homonal therapy among non-metropolitan women⁴⁰ being reported.

Non-metropolitan women were consistently (12-58%) less likely to undergo sentinel node biopsies (SNB), ⁸⁶⁻⁸⁸ or post-mastectomy breast reconstruction ⁸⁹⁻⁹² with only one earlier study reporting no difference in reconstruction rates. ⁹³ They also had a 10% higher risk of unplanned readmissions. ⁹⁴ However, no geographical variations in axillary node surgery ^{77 79 83} or access to specialist breast care nurses were evident. ^{95 96}

Of the seven included studies comprising non-metropolitan women only, one reported that breast care nurses were important in ensuring continuity of care, ⁹⁷ two found a high level of patient satisfaction with the treatment decision process ⁹⁸ ⁹⁹ and one found that geographical setting was no impediment to receiving breast conserving surgery or to accessing multidisciplinary care at a single non-metropolitan treatment centre. ¹⁰⁰ Among regional women in the state of New South Wales, breast conserving surgical rates increased by 9% after a publicly funded radiotherapy service became available in 2013, compared to earlier years when the only options were a local private or publicly funded out-of-areas service. ¹⁰¹ However, regional women who lived ≥100-200 km away (versus <100 km) from a radiotherapy service were twice as likely to have a mastectomy. ¹⁰²

The only study examining geographical variations in clinical management for advanced breast cancer found no geographical variations in mastectomy rates among women with metastatic disease.⁷⁴

Recommended clinical management

Nine (four high, five moderate quality) of 15 included studies reported geographical variations in guideline-concordant care with non-metropolitan women being less likely to undergo adjuvant radiotherapy, 50 54 73 84 hormonal therapy⁴⁰ or sentinel node biopsies⁸⁶⁻⁸⁸ and more likely to experience longer delays in commencing adjuvant chemotherapy. 56 However the other six studies (two high, two moderate, two low quality) found no significant geographical variations in receipt of recommended care. 77 79 80 83 85 95

Referral

Non-metropolitan women were less likely to be referred to a radiation oncologist, ⁸⁰ and were more likely to experience delays in assessment by a medical oncologist. ⁵⁶ Further, in a cross-sectional survey of 70 non-metropolitan women, 42% were referred to another health professional before surgery. ⁹⁹ All studies were of moderate quality.

International studies have consistently shown geographical variations in access to high volume surgical care $^{103-105}$ and provided clear evidence that such care is related to improved breast-cancer survival $^{104\ 106}$ and better concordance with clinical care guidelines. Hence eligible studies that described access to high caseload surgeons were also considered for this clinical question. One high-quality study reported that non-metropolitan women were 9% more likely to be treated locally by low caseload surgeons 26 (defined as ≤ 10 or ≤ 20 cases/year) with similar findings reported by three other high quality studies. $^{40\ 50\ 78}$

Treatment completion

Of the two included studies one found that non-metropolitan women were more likely to complete prescribed chemotherapy than metropolitan women. Another reported that women treated by low caseload surgeons (\leq 20 cases/year) were more likely to decline clinician recommended surgery, radiotherapy or chemotherapy based on data from the National Breast Cancer Audit.

The review did not identify any studies examining geographical variations in the specific treatment options offered to non-metropolitan and metropolitan Australian female breast cancer patients, or post-treatment follow-up according to current national guidelines.¹¹⁰

Discussion

This review found consistent evidence for variations in survival and clinical management, limited evidence for variations in diagnostic outcomes and inconsistent evidence for variations in tumour characteristics by residential location of Australian female breast cancer patients.

While gaps in the literature limited our ability to draw clear links between identified variations and the drivers of these variations, there was good evidence that poorer breast cancer survival (at least up to five years after diagnosis) for non-metropolitan women reflects more advanced disease at diagnosis, greater comorbidities, treatment-related factors and area-level disadvantage. ^{29 33 37 40-44}
According to the recent systematic review by the International Agency for Research on Cancer (IARC)¹¹¹ there is sufficient evidence for the efficacy of mammographic screening in reducing breast-cancer mortality for women aged 50 to 69 years. In Australia, increasing participation for groups with low screening rates can be achieved through the existing and well established population-based national mammographic program (BreastScreen). Targeted strategies are required including thorough engagement and communication with primary care to improve screening participation rates. ⁶⁰ It is possible that these survival patterns are impacted by the lead time caused by mammographic screening; ¹¹² while we found only limited evidence that participation in the publicly funded BreastScreen services varies by geographical area, the lack of data on the number of privately screened women precludes an evaluation of actual population-based screening participation and its

impact on the observed survival patterns. Hence it remains a priority to explore means to combine data on public and private screening to gain more comprehensive information on total rates of breast cancer screening nationally.

The review found a consistent pattern of geographical variations in patterns of care and lower receipt of optimal clinical management for early breast cancer among non-metropolitan women in Australia. Reasons for these variations likely included limited access to oncological services and multidisciplinary care. Regional Cancer Centres across Australia and integrated cancer networks were established to improve access to oncological care for regional patients. However overcoming barriers to multidisciplinary care, considered best practice in breast cancer care, I15-117 in regional areas remains a challenge. Multidisciplinary cancer teams (MDT) are sparse outside metropolitan areas and vary widely in the disciplines represented within existing teams.

The efficacy of MDT's in informed clinical decision making, coordinated care and evidence-based practice for breast cancer patients has been well documented. Several of the included studies in this review identified limited access to MDT care for non-metropolitan women as a possible contributor to lower receipt of guideline concordant care, It is possible that the major benefits of MDT lie, in part, with greater adherence to standard therapy, which may indirectly impact clinical outcomes.

The evidence for the impact of MDT on breast cancer survival is more limited, possibly reflecting methodological limitations and heterogeneity in MDT definitions. ¹²⁰ However, surgical specialization has been shown to be associated with improved survival, ¹⁰⁶ and we found that non-metropolitan women had consistently poorer access to high-volume surgeons ²⁶ ⁴⁰ ⁵⁰ ⁷⁸ which in Australia are predominantly based in major cities. ¹²³

Australian clinical practice guidelines for the management of early breast cancer recommend postoperative radiotherapy after breast conserving surgery to reduce the risk of local recurrence, adjuvant
endocrine therapy and/or chemotherapy where appropriate based on hormone receptor status, ¹²⁴ and
sentinel node biopsy offered to women with unifocal clinically node negative tumours (≤ 30mm). ¹²⁵
However this review found limited but consistent evidence for geographical variations in receipt of
care according to these guidelines. Specifically, non-metropolitan women were less likely to undergo
adjuvant radiotherapy, ^{40 50 54 73 84} hormonal therapy, ⁴⁰ or SNB. ⁸⁶⁻⁸⁸ Lower utilization of SNB in nonmetropolitan areas may reflect inadequate access to necessary resources, less relevant training and
experience in performing SNB among general surgeons outside major treatment centres ^{87 88} and lack
of interdiscliplinary collaboration required to perform SNB's. ⁸⁶⁻⁸⁸ Surgeon-level interventions may be
required to help improve sentinel node biopsy rates and hence quality of care and reduced morbidity.

The finding that non-metropolitan women were less likely to receive adjuvant radiotherapy likely reflects variations in access to such facilities. The Water it should be acknowledged that all included studies were published in the period 1st January 1990 to November 2017 and that some earlier studies may not reflect current practice and/or the impact of improved access to radiation services with the development of new radiotherapy infrastructure in regional Australia over the last five years. Both service affordability and availability impact radiotherapy utilization with the uptake of breast conserving surgery among regional women increasing after provision of a publicly funded local radiotherapy service. Similar patterns were also reported for radiotherapy utilization among all regional cancer patients. Similar patterns were also reported for radiotherapy utilization among all regional cancer patients. The waiting time from radiation oncologist assessment to recieiving radiotherapy (for any cancer) has also improved over time. Although implementation of routine reporting of waiting times from diagnosis to commencing radiotherapy by geographical location would help identify when and where delays in referral and commencing treatment occur.

Given the potential survival benefits of adjuvant radiotherapy, ¹³⁰ ¹³¹ the lower utilization of radiotherapy among non-metropolitan women ⁴⁰ ⁵⁰ ⁵⁴ ⁷³ and those with poorer access to radiotherapy facilities ⁷³ ⁸⁴ ¹⁰² is of concern.

Although some recent Queensland-based studies found limited evidence for a temporal reduction in geographical variations for breast cancer stage⁵³ and surgical patterns,⁷⁸ in practice these changes were subtle and although the non:metropolitan: metropolitan differential reduced, it was still evidence in the most recent time period. Moreover, despite improvements in survival over all areas in Queensland over time, geographical inequalities remained.^{34 36} These studies highlight the importance of ongoing monitoring of measured outcomes along breast cancer continuum to assess whether there has been a definitive change in these variations and to identify key drivers of any changes.

While the review found consistent evidence for variations in breast cancer survival and clinical management, patterns were inconsistent for other outcomes, primarily due to heterogeneity of the included studies or in some cases a lack of studies. These findings emphasise the importance of the work of Cancer Australia (Australia's national cancer control agency) in establishing a national comprehensive system for recording breast cancer stage and clinical management at the population level thereby enabling accurate monitoring of the effectiveness of strategies and initiatives to improve breast cancer outcomes for non-metropolitan women in Australia.

On an international scale, inequities in access to specialised care¹⁰³⁻¹⁰⁵ and geographical variations across the breast cancer continuum including screening,⁷ stage at diagnosis⁹ ¹³² and patterns of care⁸ ¹⁰⁸ ¹³²⁻¹³⁷ are well documented. There is widespread consensus that these variations reflect a combination of socio-economic, demographic and environmental factors including geography, comorbidities, access, treatment and stage at diagnosis that defy easy solutions.⁷⁻⁹ ¹⁰⁴ ¹⁰⁵ ¹³² ¹³⁶ The persistence of such

inequities even for universal (publicly-funded) health-care systems^{7 104 132 134 137} highlights the complexity of the underlying issues.

Limitations

A number of issues made direct comparisons and to some extent interpretation of findings across studies particularly challenging. The assessment of comparability was hampered by the wide variability in study quality, levels of evidence, methodology, data sources, time period and terminology. These issues also prevented meta-analyses being carried out. Many studies were predominantly conducted at the state-level, making the generalisation of findings to the national level difficult. The review also highlighted the need to improve and standardize definitions of geographical location to produce more uniform and reliable remoteness classifications. This would improve data comparability in terms of residential location and hence facilitate more definitive conclusions to be drawn on the strength of the available evidence. Similar concerns have been noted by international reviews on area-level variations in other cancer outcomes.⁸ 138 139

Moreover, many studies had important limitations including selection bias and inadequate follow-up that impacted their quality. While using registry data allows generalizability of findings, such studies cannot comprehensively control for all potential confounders, especially those related to individual-level socio-economic status, clinical or treatment factors since Australian cancer registries do not routinely collect information on these measures. ¹⁴⁰ Hence population-based studies can adjust for area-level socio-economic status but not between-persons differences. Only cross-sectional studies, although deemed inferior to population-based studies in terms of representativeness, can collect information on individual-level measures.

Considerable efforts were made to conduct a comprehensive search of existing literature on specified clinical questions by searching multiple databases with complex queries and evaluating reference lists of identified articles, published reviews and government reports to find additional articles. However, it is still possible that the search term criteria used could have unintentionally resulted in exclusion of relevant articles. Included articles were also limited to those indexed in the accessed databases.

Conclusions

By examining the current evidence relating to geographical variations in breast cancer outcomes across the continuum of care for Australian women, this review has important implications for clinical practice, service delivery and future research. It has highlighted the gap in knowledge of variations in the treatment of advanced breast cancers, patient decision making and post-treatment follow-up.

While addressing the geographical variations in breast cancer survival and clinical management will require a multifaceted approach, initial efforts could include improving access to and participation in breast screening programs, raising awareness of the benefits of early detection and enabling all women diagnosed with breast cancer to be assessed by a multidisciplinary team that considers all relevant treatment options and have access to best practice treatment. To achieve equitable access for all women, it is crucial to promote coordinated care among non-metropolitan women and initiatives to facilitate the educational diffusion of health care changes among clinicians and patients through emerging technologies¹⁴¹ to overcome barriers of distance. Recognising the heterogeneity of existing studies in terms of geographical coverage and definitions, the establishment of a national comprehensive system for recording breast cancer stage and clinical management would enable accurate monitoring of the success of these initiatives.

Finally, encouraging evidence-based research aimed at better understanding the reasons for geographical variations in breast cancer management and outcomes at each stage of the continuum of care needs to be a priority to inform the development of targeted initiatives to improve survival and quality of life for rural and remote women with breast cancer in Australia.



Funding

This project was funded by Cancer Australia. Dr Philippa Youl and Professor Gail Garvey are funded by a National Health and Medical Research Council Early Career Fellowship (#1054038 and #1105399 respectively).

Conflict of Interest

The authors report no conflict of interest.

Authors Contributions

All authors, PY, PB, PD, DY, JA, GG, IW, JC and HZ contributed to the design of the study. PY and PB coordinated the study; PD conducted the literature searches and drafted the manuscript; PD, PY, DY and PB all acted as reviewers and participated in data collection; PY, PB, DY, JA and GG contributed to the initial draft of the manuscript and all authors, PY, PB, PD, DY, JA, GG, IW, JC and HZ refined and approved the final version of the paper.

Acknowledgements

The project was commissioned and funded by Cancer Australia. The authors would like to acknowledge the advice of the Project Steering Committee.

Data sharing statement

No additional data are available

Patient consent

Not relevant

Figure legends

Figure 1: Process of inclusion and exclusion of studies for the systematic review

Supplementary files

Supplementary file 1 Database-specific search queries by individual clinical questions.

Additional file 1 lists search queries for the searched databases by each of the individual clinical questions in numerical order.

File name: Supplementary file 1.pdf

Supplementary file 2 Quality appraisal tools for included quantitative studies. Additional file 2 shows the scoring system used for quality appraisal of the included quantitative studies.

File name: Supplementary file 2.pdf

Supplementary file 3 Excluded studies with reasons for exclusion. Additional file 3 lists the excluded studies with reasons for exclusion in alphabetical order by author.

File name: Supplementary file 3.pdf

Supplementary file 4 Detailed characteristics of the included studies by three key themes.

Additional file 4 presents detailed characteristics on included studies by key themes of survival outcome, patient and tumour characteristics and diagnostic and treatment outcomes

File name: Supplementary file 4.pdf

Table 1: Clinical questions guiding the systematic review

Survival Outcomes

1. In women diagnosed with breast cancer, do non-metropolitan women have poorer breast cancer survival compared to metropolitan women in Australia?

Patient and Tumour Characteristics

- 2. In women diagnosed with breast cancer, do non-metropolitan women have different socio-demographic characteristics compared to metropolitan women in Australia?
- 3. In women diagnosed with breast cancer, do non-metropolitan women have more advanced tumour characteristics compared to metropolitan women in Australia?

Diagnostic and Treatment Outcomes

- 4. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to access breast screening services compared to metropolitan women in Australia?
- 5. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to adhere to recommended breast screening intervals (2 yearly) compared to metropolitan women in Australia?
- 6. In women diagnosed with breast cancer, are there differences in the clinical management between non-metropolitan and metropolitan women in Australia?
- 7. In women diagnosed with breast cancer, are non-metropolitan women less likely to receive the recommended clinical management compared to metropolitan women in Australia?
- 8. In women diagnosed with breast cancer, are non-metropolitan women more likely to experience delays in referral to breast cancer specialist clinicians compared to metropolitan women in Australia?
- 9. In women diagnosed with breast cancer, do non-metropolitan women experience fewer treatment options compared to metropolitan women in Australia?
- 10. In women diagnosed with breast cancer, are non-metropolitan women less likely to complete prescribed treatment compared to metropolitan women in Australia?
- 11. In women diagnosed with breast cancer, are non-metropolitan women less likely to participate in recommended follow-up compared to metropolitan women in Australia?

Table 2: Summary scores, overall grades and Levels of evidence for included studies

Study	Metropolitan/non-metropolitan	Score ²	Score ² Quality ³	
A 1 1 1 100 7 74	definition	1.5	TT' 1	ш. 2
Adelson <i>et al</i> 1997 ⁷⁴	Based on health services	15	High	III-3
Ahern et al 2015 ⁸⁵	ARIA+ Remoteness Index	7	Low	IV
Ahern <i>et al</i> 2016 ⁹⁵	ARIA+ Remoteness Index	7	Low	IV
AIHW 2013 ²⁸	ARIA+ Remoteness Index	14.5	High	II
Azzopardi et al 2014 ⁷³	ASGC	9	Moderate	II
Baade <i>et al</i> 2011 ⁵²	ARIA+ Remoteness Index	16.5	High	II
Baade <i>et al</i> 2016 ⁷⁸	Distance to radiation treatment facilities	16	High	II
Barratt et al 1997 ⁶³	RRMA Classification	9.5	Moderate	II
Bell et al 2012 ⁸⁹	Postcodes ¹	15	High	II
Bonnet et al 1990 ³⁰	Postcodes ¹	14.5	High	II
Budden et al 2014 ⁹⁸	N/A: regional women only	10	Moderate	IV
Campbell et al 2006 ⁹⁶	Based on residential area	9.5	Moderate	III-3
Chen et al 2015 ³¹	ARIA+ Remoteness Index	15.5	High	II
Clayforth et al 2007 ³²	Postcodes ¹	15	High	II
Cockburn et al 1997 ⁶⁸	N/A: rural and remote women only	10	Moderate	III-3
Chong et al 201586	ASGC	13	Moderate	III-3
Collins <i>et al</i> 2017 ¹⁰²	N/A: regional women only	14	High	II
Craft et al 1997 ⁷⁹	RRMA Classification	12	Moderate	III-3
Cramb <i>et al</i> 2012 ³³	Distance to radiation treatment facilities	15.5	High	II
Cramb <i>et al</i> 2016a ³⁵	ASGC	14	High	II
Cramb <i>et al</i> 2016b ³⁴	ASGC	15	High	II
Cramb <i>et al</i> 2017 ³⁶	ASGS	15	High	II
Dasgupta et al 2012 ³⁷	ARIA	16.5	High	II
Dasgupta et al 2017a ⁵³	Distance to radiation treatment facilities	16	High	II
Dasgupta et al 2017b ⁸⁷	Distance to radiation treatment facilities	16	High	II
Dasgupta et al 2017c ⁹⁰	Distance to radiation treatment facilities	16	High	II
Depczynski, et al 2017 ⁵⁵	ARIA+ Remoteness Index	13	Moderate	III-3
Eley <i>et al</i> 2008 ⁹⁷	N/A: rural and remote women only	7.5	Low	IV
Flitcroft et al 2016 ⁹¹	ARIA+ Remoteness Index	10	Moderate	III-3
Fox <i>et al</i> 2013 ⁵⁶	RRMA Classification	10.5	Moderate	III-3
Hall & Holman 2003 ⁹³	ARIA	14.5	High	II
Hall et al 2004a ³⁸	ARIA	15	High	II
Hall <i>et al</i> 2004b ⁸¹	ARIA	14.5	High	II
Hill <i>et al</i> 1994 ⁸⁰	Postcodes ¹	12.5	Moderate	II
Hsieh <i>et al</i> 2014 ⁴⁹	ARIA+ Remoteness Index	14	High	II
Hsieh <i>et al</i> 2015 ⁸⁴	Distance to radiation treatment facilities	14	High	II
Hsieh <i>et al</i> 2016a ³⁹	ASGC	14	High	II
Hsieh <i>et al</i> 2016b ⁴⁸	ARIA+ Remoteness Index	15	High	II
Hughes <i>et al</i> 2014 ⁶⁹	Postcodes ¹	10.5	Moderate	III-3
Kok <i>et al</i> 2006 ⁵⁴	RRMA Classification	14.5	High	III-3
Koshy <i>et al</i> 2005 ⁸²	Postcodes ¹	9.5	Moderate	III-3
Kricker et al 2001 ⁸³	Unclear	16	High	III-3
Lai et al 2007 ⁹⁴	RRMA Classification	15	High	II
Lam et al 2015 ¹⁰¹	N/A: regional women only	10	Moderate	IV
Lam & 41 2013	14/11. Tegional women only	10	Moderate	1 4

Study	Metropolitan/non-metropolitan	Score ²	Quality ³	Level ⁴
•	definition		_ ,	
Leung <i>et al</i> 2014 ⁶¹	ARIA+ Remoteness Index	12.5	Moderate	III-3
Leung <i>et al</i> 2015 ⁶²	ARIA+ Remoteness Index	12	Moderate	III-3
Leung <i>et al</i> 2016 ⁵⁸	ARIA+ Remoteness Index	13	Moderate	III-3
Lord <i>et al</i> 2012 ⁵⁷	ARIA	14	High	II
Luke <i>et al</i> 2004 ⁵⁹	Postcodes ¹	14	High	II
Martin <i>et al</i> 2006 ⁷⁵	Based on residential area	14.5	High	II
Mastaglia & Kristjanson 2001 ⁷⁶	Unclear	6.5	Low	IV
Mitchell et al 2006 ⁴⁰	Postcodes ¹	16	High	II
Morris <i>et al</i> 2012 ⁸⁸	ASGC	10.5	Moderate	III-3
O'Byrne <i>et al</i> 2000 ⁷⁰	RRMA Classification	15.5	High	III-3
Ristevski et al 2012 ⁹⁹	N/A: regional women only	9	Moderate	IV
Roder et al 2012a ²⁹	ASGC	14.5	High	III-3
Roder <i>et al</i> 2012b ¹⁰⁹	ASGC	14	High	III-3
Roder et al 2013a ⁵⁰	ASGC	14	High	III-3
Roder et al 2013b ²⁶	ASGC	14.5	High	III-3
Roder et al 2013c ⁹²	ASGC	14.5	High	III-3
Roder <i>et al</i> 2014 ⁵¹	ASGC	15	High	III-3
Schofield et al 1994 ⁶⁶	Distance to screening services	10.5	Moderate	II
Siapush & Singh 2002 ⁶⁷	Based on residential area	12.5	Moderate	II
Spilsbury et al 2005 ⁴¹	Postcodes ¹	16	High	II
Sullivan et al 2003 ⁶⁴	Postcodes ¹	11	Moderate	III-3
Supramaniam et al 2014 ⁴²	ARIA+ Remoteness Index	17	High	II
Taylor 1997 ⁴⁷	capital city, other metropolitan, rural	14.5	High	II
Tervonen et al 2017 ⁴³	ARIA+ Remoteness Index	14	High	II
Thompson et al 2008 ⁷⁷	ARIA+ Remoteness Index	14.5	High	II
Tracey et al 2008 ⁴⁴	ARIA	15	High	II
Tulloh & Goldsworthy 1997 ¹⁰⁰	N/A: rural and remote women only	7	Low	III-3
Weber <i>et al</i> 2014 ⁶⁵	ARIA+ Remoteness Index	10.5	Moderate	III-3
Wilkinson & Cameron 2004 ⁴⁶	Postcodes ¹	9.5	Moderate	II
Yu et al 2015 ⁴⁵	ARIA+ Remoteness Index	12	Moderate	II

ARIA Accessibility/Remoteness Index of Australia; ASGC Australian Standard Geographical Classification; ASGS Australian Standard Geographical Standard; N/A Not applicable; RRMA Rural, Remote and Metropolitan Areas

- 1. Postcodes within state capital were considered metropolitan, remaining were non-metropolitan
- 2. Average score over scores from two independent reviewers. Please refer to text for further details.
- Quality categories: High (score14-18), Moderate (score 9-13.5) or Low (score <9); please refer to text for further details.
- Australian National Health and Medical Research Council (NHMRC) ²⁴ levels of evidence in decreasing order of strength are Level II, Level III-1, Level III-2, Level III-3 and Level IV.

Table 3 Summary of included studies on differentials in breast cancer survival outcomes by residential location

Author, year	Location ¹	Period (follow-up)	Sample size	Po	orer survival
				Unadjusted	Adjusted ²
AIHW 2013 ²⁸	National	1982-2007 (end 2010)	NS	Non-metropolitan	NR
Wilkinson & Cameron 2004 ⁴⁶	SA	1977-1993 (to 2000)	NS	Non-metropolitan	NR
Cramb <i>et al</i> 2012 ³³	Qld	1996-2007	25,202	Non-metropolitan	No difference (s, d)
Dasgupta et al 2012 ³⁷	Qld	1997-2006 (end 2007)	18,568	Non-metropolitan	No difference (s, d)
Hsieh et al 2016b ⁴⁸	Qld	1997-2007 (end 2008)	9,741	Non-metropolitan	No difference (s, d)
Tervonen et al 2017 43	NSW	1980-2008 (end 2009)	88,768	Non-metropolitan	No difference (s, d)
Tracey et al 2008 ⁴⁴	NSW	1980-2003 (end 2004)	59,731	Non-metropolitan	No difference (s, d)
Mitchell et al 2006 ⁴⁰	WA	1999 (end 2004)	899	Non-metropolitan	No difference (s, t)
Supramaniam et al 2014 ⁴²	NSW	2001-2007 (end 2008)	27,850	Non-metropolitan	No difference (s, d, t, c)
Roder et al 2012a ²⁹	National	1991-2006	62,082	Non-metropolitan	No difference (d)
Hall <i>et al</i> 2004a ³⁸	WA	1991-2001	7,117	Non-metropolitan	No difference (d, t, c)
Spilsbury et al 2005 ⁴¹	WA	1982-2000	11,445	Non-metropolitan	No difference (d, t, c)
Taylor 1997 ⁴⁷	NSW	1980-1991 (end 1992)	25,793	No difference	No difference (s)
Bonnet <i>et al</i> 1990 ³⁰	SA	1980-1986 (end 1988)	2,565	Non-metropolitan	Non-metropolitan (s)
Chen <i>et al</i> 2015 ³¹	NSW	2000-2008	36,867	Non-metropolitan	Non-metropolitan (s)
Cramb <i>et al</i> 2016a ³⁵	Qld	1997-2011	NS	Non-metropolitan	Non-metropolitan (s)
Cramb et al 2016b ³⁴	Qld	1997-2011	34,231	Non-metropolitan	Non-metropolitan (s)
Hsieh et al 2014 ⁴⁹	Qld	1997-2007 (end 2008)	23,766	Non-metropolitan	Non-metropolitan (s, d)
Hsieh et al 2016a ³⁹	Qld	1997-2007 (end 2008)	23,766	Non-metropolitan	Non-metropolitan (s)
Yu et al 2015 ⁴⁵	NSW	1987-2007 (end 2007)	63,757	Non-metropolitan	Non-metropolitan (s, d)
Clayforth et al 2007 ³²	WA	1989, 1994, 1999 (end 2005)	1,729	Non-metropolitan	Non-metropolitan (s, t)
Cramb <i>et al</i> 2017 ³⁶	Qld	1997-2004 (end 2005); 2005-2012 (end 2013)	38,204	Non-metropolitan	Non-metropolitan

NR not relevant, NS not stated

^{1.} National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia and WA Western Australia

^{2.} All adjusted for age except Bonnet et al 1990³⁰

⁽s) Also adjusted for some measure of spread of diagnosis, such as stage at diagnosis or tumour diameter

⁽t) Also adjusted for treatment-related factors

⁽d) Also adjusted for area-disadvantage

⁽c) Also adjusted for comorbidities

Table 4 Summary of included studies on differentials in patient and tumour characteristics by residential location

Author, year	Location ¹	Period	Sample size	Finding ²
	Patient character	istics (higher ar	ea-level socio-econ	omic disadvantage)
Roder <i>et al</i> 2013a ⁵⁰	National	1998-2010	30,299	Non-metropolitan
Roder <i>et al</i> 2014 ⁵¹	National	1998-2010	30,299	Non-metropolitan
	Tumour character	istics (higher sp	ead of disease) ³	
Bonnet <i>et al</i> 1990 ³⁰	SA	1980-1986	1,171	No difference
Depczynski, et al 2017 ⁵⁵	NSW	2006-2009	726	No difference
Fox <i>et al</i> 2013 ⁵⁶	NSW	2008-2011	400	No difference
Leung et al 2016 ⁵⁸	NSW, Qld, Vic	1997-2011	195	No difference
Lord <i>et al</i> 2012 ⁵⁷	NSW	2001-2002	6,664	No difference
Luke <i>et al</i> 2004 ⁵⁹	SA	1997-2002	4,912	No difference
Mitchell et al 2006 ⁴⁰	WA	1999	899	No difference
Wilkinson & Cameron 2004 ⁴⁶	SA	1980-1998	NS	No difference
Baade <i>et al</i> 2011 ⁵²	Qld	1997-2006	18,568	Non-metropolitan
Dasgupta et al 2017a ⁵³	Qld	1997-2014	38,706	Non-metropolitan
Kok <i>et al</i> 2006 ⁵⁴	Vic	1993-2000	5,294	Non-metropolitan
Roder et al 2013b ²⁶	National	1998-2010	30,299	Non-metropolitan
Tracey et al 2008 ⁴⁴	NSW	1980-2003	59,731	Metropolitan

NS not stated

National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia; Vic: Victoria and WA Western Australia

^{2.} Some measure of spread of disease such as stage at diagnosis or tumour size.

Table 5 Summary of included studies on differentials in diagnostic outcomes by residential location

Author, year	Location ¹	Period	Sample size ²	Finding		
	Higher screening rate ³					
Barratt et al 1997 ⁶³	National	1996	1,035	No difference		
Leung <i>et al</i> 2014 ⁶¹	National	2001-2010	11,200	No difference.		
Leung <i>et al</i> 2015 ⁶²	National	2010	10,011	No difference		
Sullivan et al 2003 ⁶⁴	WA	1982-2000	380	Non-metropolitan		
Weber <i>et al</i> 2014 ⁶⁵	NSW	2006-2010	101,063	Non-metropolitan		
Schofield et al 1994 ⁶⁶	Vic	1988-1990	668	Metropolitan		
Siapush & Singh 2002 ⁶⁷	National	1995	10,179	Metropolitan		
Cockburn et al 1997 ⁶⁸	Vic	1995	180 non-	No screening history and knowing		
			metropolitan	service locations screening predictors		
		Higher resc	reening rate⁴	-		
Hughes et al 2014 ⁶⁹	WA	1999-2008	NS	No difference		
Leung <i>et al</i> 2014 ⁶¹	National	2001-2010	11,200	Non-metropolitan		
Leung <i>et al</i> 2015 ⁶²	National	2010	10,011	Non-metropolitan		
O'Byrne <i>et al</i> 2000 ⁷⁰	Vic	1995-1996	121,889	Non-metropolitan		
Siapush & Singh 2002 ⁶⁷	National	1995	10,179	Metropolitan		

- 1. National: all states/territories; NSW: New South Wales; Vic: Victoria and WA Western Australia
- 2. Only aged 50-69 years who were eligible at time of this review and all included studies for publicly funded BreastScreen program in Australia
- 3. Having had at least one screening mammogram
- 4. Having another screening mammogram within two years of the initial screen

Table 6 Summary of included studies on differentials in treatment outcomes by residential location

Author, year	Location ¹	Period	Sample size	Finding	

Koshy <i>et al</i> 2005 ⁸²	NOW ACT	Higher mastector		N. 1:00	
Kricker et al 2005 Kricker et al 2001 ⁸³	NSW, ACT	1997-2002 1992, 1995	1,069	No difference No difference	
Kricker et at 2001	NSW	1992, 1993	2,020 or 2,883	No difference	
Adelson et al 1997 ⁷⁴	NSW	1991-1992	4,038	Non-metropolitan	
Azzopardi <i>et al</i> 2014 ⁷³	National	1998-2012	21,643	Non-metropolitan	
Martin <i>et al</i> 2006 ⁷⁵	WA	1990-1999	2,713	Non-metropolitan	
Mastaglia & Kristjanson 2001 ⁷⁶	WA	1996-1997	160	Non-metropolitan	
Roder et al 2013b ²⁶	National	1998-2010	30,299	Non-metropolitan	
Thompson et al 2008 ⁷⁷	Qld	2004-2005	1,274	Non-metropolitan	
	-	Higher breast cor	serving sui	rgery	
Hall <i>et al</i> 2004b ⁸¹	WA	1991-2000	7,304	No difference	
Adelson et al 1997 ⁷⁴	NSW	1991-1992	4,038	Metropolitan	
Azzopardi <i>et al</i> 2014 ⁷³	National	1998-2012	21,643	Metropolitan	
Baade <i>et al</i> 2016 ⁷⁸	Qld	1997-2011	11,631	Metropolitan	
Craft <i>et al</i> 1997 ⁷⁹	National	1993	4,683	Metropolitan	
Hill <i>et al</i> 1994 ⁸⁰	Vic	1990	856	Metropolitan	
Kok <i>et al</i> 2006 ⁵⁴	Vic	1993-2000	5,294	Metropolitan	
Mitchell et al 2006 ⁴⁰	WA	1999	899	Metropolitan	
Roder <i>et al</i> 2013a ⁵⁰	National	1998-2010	30,299	Metropolitan	
	•	Lower radiothera	ıpy		
Azzopardi <i>et al</i> 2014 ⁷³	National	1998-2012	21,643	Non-metropolitan	
Hsieh <i>et al</i> 2015 ⁸⁴	Qld	1997-2008	6,357	Non-metropolitan	
Kok <i>et al</i> 2006 ⁵⁴	Vic	1993-2000	5,294	Non-metropolitan	
Mitchell et al 2006 ⁴⁰	WA	1999	899	Non-metropolitan	
Roder <i>et al</i> 2013a ⁵⁰	National	1998-2010	30,299	Non-metropolitan	
0.5		ower hormonal th	erapy		
Ahern <i>et al</i> 2015 ⁸⁵	National	2013	325	No difference	
Hsieh et al 2015 ⁸⁴	Qld	1997-2008	6,357	No difference	
Mitchell et al 2006 ⁴⁰	WA	1999	899	Non-metropolitan	
84		ower chemotherap			
Hsieh <i>et al</i> 2015 ⁸⁴	Qld	1997-2008	6,357	No difference	
Hill et al 1994 ⁸⁰	Vic	1990	856	No difference	
Mitchell <i>et al</i> 2006 ⁴⁰	WA	1999	899	No difference	
Roder <i>et al</i> 2013a ⁵⁰	National	1998-2010	30,299	Metropolitan	
CI 1201586		wer sentinel node		37	
Chong et al 2015 ⁸⁶	National	2008-2010	18,737	Non-metropolitan	
Dasgupta et al 2017b ⁸⁷	Qld	July 2008- December 2012	5,577	Non-metropolitan	
Morris <i>et al</i> 2012 ⁸⁸	National		1 267 to	Non-metropolitan	
Mons et at 2012	National	2008 (last 6	1,267 to	Non-metropontan	
Craft et al 1997 ⁷⁹	National	Lower axillary sur 1993	gery 4,683	No difference	
Kricker et al 2001 ⁸³	NSW	1993 1992, 1995	4,083 2,020 or	No difference	
MICKEI Et al 2001	TAPAA	1774, 1773	2,020 or 2,883	140 difference	
Thompson et al 2008 ⁷⁷	Qld	2004-2005	1,274	No difference	
1		ver breast reconsti		_	
Hall & Holman 2003 ⁹³	WA Lo	1991-2000	7,303	No difference	
Bell <i>et al</i> 2012 ⁸⁹	Vic	2004-2006	366	Non-metropolitan	
Dasgupta et al 2017c ⁹⁰	Qld	1997-2012	4,104	Non-metropolitan	
2 40 5 up at at 201 / C	ζ.ω	1771 2012	1,101	1.01 metropontum	

Author, year	Location ¹	Period	Sample size	Finding
Flitcroft et al 2016 ⁹¹	National	2013	3,786	Non-metropolitan
Roder et al 2013c ⁹²	National	1998-2010	12,207	Non-metropolitan
	Hig	her unplanned a	dmisisons	
Lai <i>et al</i> 2007 ⁹⁴	WA	1995-1999	2,703	Non-metropolitan
Access breast care nurses				
Ahern <i>et al</i> 2016 ⁹⁵	National	2013	902	No difference
Campbell et al 2006 ⁹⁶	National	1997	544	No difference
	I	Longer treatment	delays	
Fox <i>et al</i> 2013 ⁵⁶	NSW	2008-2011	400	Non-metropolitan
		Poorer quality of	f care	
Hill <i>et al</i> 1994 ⁸⁰	Vic	1990	856	Non-metropolitan
Fox <i>et al</i> 2013 ⁵⁶	NSW	2008-2011	400	Non-metropolitan
Baade <i>et al</i> 2016 ⁷⁸	Qld	1997-2011	11,631	Non-metropolitan
Mitchell et al 2006 ⁴⁰	WA	1999	899	Non-metropolitan
Roder <i>et al</i> 2013a ⁵⁰	National	1998-2010	30,299	Non-metropolitan
Roder <i>et al</i> 2013b ²⁶	National	1998-2010	30,299	Non-metropolitan
54		Treatment comp		
Fox et al 2013 ⁵⁶	NSW	2008-2011	400	Non-metropolitan more likely to complete chemotherapy
Roder <i>et al</i> 2012b ¹⁰⁹	National	1998-2005	36,775	Non-metropolitan less likely to follow clinician recommended treatments
		Non-metropol	itan	
Budden et al 2014 ⁹⁸	Qld	NS	104	High level satisfaction with treatment decisions
Eley <i>et al</i> 2008 ⁹⁷	Qld	2005-2006	51	Breast cancer nurses important source of care
Ristevski et al 2012 ⁹⁹	Vic	NS	70	High level satisfaction with treatment decisions
Tulloh & Goldsworthy 1997 ¹⁰⁰	Vic	1992-1995	28	Rural setting did not influence quality of care
Lam et al 2015 ¹⁰¹	NSW	2010-2014	574	A locally available publicly funded radiotherapy service increased breast conserving surgery uptake.
Collins et al 2017 ¹⁰²	Vic	2009-2014	1,213	Access to radiotherapy impacts surgical management

^{1.} National: all states/territories; NSW: New South Wales; Vic: Victoria and WA Western Australia

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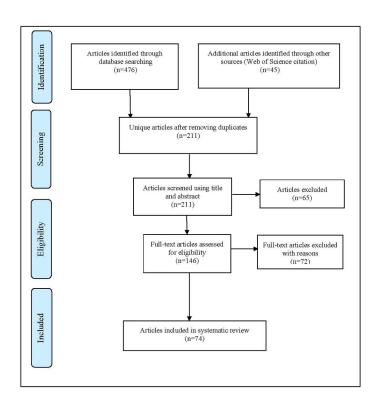


Figure 1 143x186mm (300 x 300 DPI)

Additional file 1 Database-specific search queries by individual clinical questions

Electronic databases searched: PubMed (1990- November Week 4, 2017), EMBASE (1990- November Week 4, 2017) and CINAHL (1994- November Week 4, 2017)

All search queries were conducted in a stepwise manner by breaking down each question into key concepts. Each numbered step in Tables below corresponds to the query used for an individual element such as Breast Cancer or Australia. For each element, alternative terms were used to cover all possible synonyms for that component. Finally, the individual search queries were combined to create the final search query using BOOLEAN operators such as "AND" or "OR".

1. In women diagnosed with breast cancer, do non-metropolitan women have poorer breast cancer survival compared to metropolitan women in Australia?

PUBMED search query

Search	Query						
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])						
#2	("australia"[MeSH Terms] OR Australia/epidemiology)						
#3	((((((((((((((((((((((((((((((((((((((
#4	(((((((("survival"[MeSH Terms]) OR mortality[MeSH Terms]) OR "survival rate"[MeSH Terms]) OR "disease free survival"[MeSH Terms]) OR excess mortality[MeSH Terms]) OR survival analyses[MeSH Terms]) OR survival analyses[MeSH Terms]) OR survival analyses[MeSH Terms]						
#5	((((((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND (((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

EMBASE search query (via EBSCO host)

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'survival'/exp OR 'survival' OR 'cancer mortality'/exp OR 'cancer mortality'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('survival'/exp OR 'survival' OR 'cancer mortality'/exp OR 'cancer mortality') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Survival") OR (MH "Survival Analysis+") OR (MH "Mortality+") OR TX 'survival'
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

2. In women diagnosed with breast cancer, do non-metropolitan women have different socio-demographic characteristics compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))))))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology)))))))))))))))))))))))))))))))))))

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'demography'/exp OR 'demography' OR 'socioeconomics'/exp OR 'socioeconomics' OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health disparity' OR 'health care disparity'
#4	(age OR 'risk factor' OR 'lifestyle' OR 'health insurance' OR 'comorbidity') AND ('incidence'/exp OR 'incidence')
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'demography'/exp OR 'demography' OR 'socioeconomics'/exp OR OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health disparity' OR 'health care disparity'/exp OR 'health disparity' OR 'health disparity'/exp OR 'incidence' OR 'lifestyle' OR 'health insurance' OR 'comorbidity') AND ('incidence'/exp OR 'incidence') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)

Search	Query
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural
	Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare
	Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Middle Age") OR (MH "Age Factors") OR (MH "Life Style+") OR (MH "Risk Factors+") OR (MH "Insurance, Health+") OR (MH "Insurance, Health+") OR (MH "Marital
	Status+") (MH "Demography+") OR (MH "Residence Characteristics+") OR (MH "Geographic Factors") OR (MH "Comorbidity") OR "comorbidities"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

3. In women diagnosed with breast cancer, do non-metropolitan women have more advanced tumour characteristics compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'
#4	'cancer staging'/exp OR 'cancer staging' OR 'cancer grading' OR 'cancer size' OR 'metastasis'/exp OR 'metastasis'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference'/exp OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity') AND ('cancer staging'/exp OR 'cancer staging' OR 'cancer grading' OR 'cancer size' OR 'metastasis'/exp OR 'metastasis') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MM "Neoplasm Staging") OR (MM "Neoplasms, Multiple Primary+") OR AB 'cancer grade' OR "cancer stage"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; Human

4. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to access breast cancer screening services compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'mammography'/exp OR 'mammography' OR 'cancer screening'/exp)
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('mammography'/exp OR 'mammography' OR 'cancer screening'/exp) AND (rate* OR utiliz*) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Healthcare Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mammography") OR (MH "Cancer Screening")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

5. In women diagnosed with breast cancer, are non-metropolitan women in the breast screening target group less likely to adhere to recommended breast cancer screening intervals (2 yearly) compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

EMBASE search query (via EBSCO host)

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography'/exp OR 'medical geography'/exp OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'mammography'/exp OR 'mammography' OR 'cancer screening'/exp)
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND ('mammography'/exp/mj OR 'mammography' OR 'cancer screening'/exp) AND (rescreen* OR second* OR return*) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mammography") OR (MH "Cancer Screening")
S6	TX rescreen* OR TX "mammography second"
S7	S3 AND S4 AND S5 AND S6; English Language; Peer Reviewed; female

6. In women diagnosed with breast cancer, are there differences in clinical management between non-metropolitan and metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'clinical practice'/exp OR 'cancer adjuvant chemotherapy'/exp OR 'cancer chemotherapy'/exp OR 'cancer radiotherapy'/exp OR 'cancer hormonal therapy'/exp OR 'mastectomy' OR 'lymph node dissection'/exp OR 'breast reconstruction'/exp OR 'breast reconstruction' OR 'cancer therapy multimodality'/exp
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'cancer adjuvant chemotherapy'/exp OR 'cancer chemotherapy'/exp OR 'cancer radiotherapy'/exp OR 'cancer hormonal therapy'/exp OR 'mastectomy'/exp OR 'mastectomy' OR 'lymph node dissection'/exp OR 'breast reconstruction'/exp OR 'breast reconstruction' OR 'cancer therapy multimodality'/exp) AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Health Services") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Mastectomy+") OR (MH "Lumpectomy") OR (MH "Chemotherapy, Cancer+") OR (MH "Chemotherapy, Adjuvant") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Adjuvant") OR (MH "Combined Modality Therapy+") OR (MH "Breast Reconstruction") OR "Surgical patterns" or "case management"
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

7. In women diagnosed with breast cancer, are non-metropolitan women less likely to receive the recommended clinical management compared to metropolitan women in Australia

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)

Search	Query
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography'/exp OR 'medical geography'/exp OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'cancer adjuvant chemotherapy'/exp OR 'cancer adjuvant chemotherapy' OR 'cancer chemotherapy'/exp OR 'cancer chemotherapy' OR 'cancer combination chemotherapy'/exp OR 'cancer combination chemotherapy' OR 'cancer radiotherapy' OR 'cancer radiotherapy' OR 'cancer hormonal therapy'/exp OR 'lymph node dissection'/exp OR 'lymph node dissection' OR 'cancer therapy'/exp OR 'sentinel node biopsy' OR 'cancer therapy multimodality'/exp OR 'cancer therapy multimodality'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity') AND ('cancer adjuvant chemotherapy'/exp OR 'cancer adjuvant chemotherapy' OR 'cancer chemotherapy' OR 'cancer combination chemotherapy'/exp OR 'cancer radiotherapy'/exp OR 'cancer radiotherapy' OR 'cancer therapy'/exp OR 'cancer therapy' OR 'cancer therapy multimodality'/exp OR 'cancer th

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"

Search	Query
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health Centers") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Centers") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Rural Health") OR (MH "Health") OR (MH "Heal
S5	(MH "Chemotherapy, Cancer+") OR (MH "Chemotherapy, Adjuvant") OR (MH "Radiotherapy, Cancer+") OR (MH "Radiotherapy, Adjuvant") OR (MH "Combined Modality Therapy+") OR (MH "Breast Reconstruction")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

8. In women diagnosed with breast cancer, are non-metropolitan women more likely to experience delays in referral to breast cancer specialist clinicians compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms]))))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'referral and consultation'/exp OR 'referral and consultation' OR 'public hospitals' OR 'private hospitals' OR (surgical AND caseload) OR 'hospital volume' OR 'surgical volume'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity') AND ('referral and consultation'/exp OR 'referral and consultation' OR 'public hospitals' OR 'private hospitals' OR (surgical AND caseload) OR 'hospital volume' OR 'surgical volume') AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH " Referral and Consultation+")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

9. In women diagnosed with breast cancer, do non-metropolitan women experience fewer treatment options compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((

Search	Query
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'patient decision making'/exp OR 'patient decision making' OR 'patient decision aid' OR 'patient delay'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity') AND 'patient decision making'/exp OR 'patient decision making' OR 'patient decision aid' OR 'patient delay' AND [english]/lim AND [female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Decision Making, Patient+")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

10. In women diagnosed with breast cancer, are non-metropolitan women less likely to complete prescribed treatment compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	(((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms]) OR Australia/epidemiology))))) ((((((((((((((((((((((((((((((((

EMBASE search query (via EBSCO host)

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'patient compliance'/exp OR 'patient compliance' OR 'treatment refusal'/exp OR 'treatment refusal'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care
	disparity/exp OR 'health care disparity') AND ('patient compliance'/exp OR 'patient compliance' OR 'treatment refusal'/exp OR 'treatment refusal') AND [english]/lim AND
	[female]/lim AND [1990-2015]/py

CINAHL search query (via EBSCO host)

Search	Query
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"
S2	(MH "Australia+")
S3	(S1 AND S2)
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural
S5	(MH "Patient Compliance+") OR (MH "Treatment Refusal")
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female

11. In women diagnosed with breast cancer, are non-metropolitan women less likely to participate in recommended follow-up compared to metropolitan women in Australia?

PUBMED search query

Search	Query
#1	(((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])
#2	("australia"[MeSH Terms] OR Australia/epidemiology)
#3	((((((((((((((((((((((((((((((((((((((
#4	((((((((((((((((((((((((((((((((((((((
#5	((((((((("breast neoplasms"[MeSH Terms]) OR Breast Tumors[MeSH Terms]) OR Breast Cancer[MeSH Terms]) OR Breast Carcinoma[MeSH Terms])))) AND ((("australia"[MeSH Terms] OR Australia/epidemiology))))) AND (((((((((((((((((((((((((((((((((((

Search	Query
#1	'breast cancer'/exp OR 'breast cancer'
#2	'australia'/exp
#3	'rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference'/exp OR 'urban rural difference' OR
	'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health care disparity'/exp OR 'health care disparity'
#4	'postoperative care'/exp OR 'postoperative care' OR 'patient care'/exp OR 'patient care' OR 'survivorship' OR 'survivorship care plan'
#5	'breast cancer'/exp OR 'breast cancer' AND 'australia'/exp/mj AND ('rural health care'/exp OR 'rural health care' OR 'rural population'/exp OR 'rural population' OR 'urban rural difference' OR 'socioeconomics'/exp OR 'medical geography'/exp OR 'medical geography' OR 'health disparity'/exp OR 'health disparity'/exp OR 'health care disparity') AND ('postoperative care'/exp OR 'postoperative care' OR 'patient care' OR 'survivorship' OR 'survivorship care plan') AND [english]/lim AND [female]/lim AND [humans]/lim

CINAHL search query (via EBSCO host)

Search	Query	
S1	(MH "Breast Neoplasms+") OR "breast neoplasm"	
S2	(MH "Australia+")	
S3	(S1 AND S2)	
S4	(MH "Population Characteristics") OR (MH "Rural Health Centers") OR (MH "Hospitals, Rural") OR (MH "Rural Population") OR (MH "Rural Health Services") OR (MH "Rural Areas") OR (MH "Rural Health") OR (MH "Rural Health Nursing") OR (MH "Socioeconomic Factors+") OR (MH "Social Determinants of Health") OR (MH "Health Care Disparities") OR (MH "Health Status Disparities") OR (MH "Health Services Needs and Demand+") OR TX geography OR TX rural	
S5	(MH "Postoperative Care+") OR (MH "Patient Care+") OR (MH "After Care")	
S6	S3 AND S4 AND S5; English Language; Peer Reviewed; female	
	Additional searches: We also searched the INFORMIT database (1994- March Week 1, 2015)	
nformit	nformit Health (Australian databases) search query	

Additional searches:

Informit Health (Australian databases) search query

Search	Query
#1	(Breast Cancer) OR (Breast Neoplasm)
#2	MH: Australia
#3	(MH:Australia) AND ((Breast Cancer) OR (Breast Neoplasm))
#4	((MH:Australia) AND ((Breast Cancer) OR (Breast Neoplasm))) AND ((ALLTERMS:rural OR geography OR (rural health) OR socioeconomic OR inequalities))

Additional file 2: Quality appraisal tools for included quantitative studies

I. Selection bias (Sample selection for cohort studies)	Score
Representative of population of interest	2
Selected group, somewhat representative	1
Highly selected, convenient or not described	0
II. Assessment (or measurement) of exposure and or confounding variables	
Secure records, independent blind assessment	2
Independent assessment un-blinded; self-reported	1
No description or unclear how exposure was assessed	0
III. Assessment (or measurement) of outcome	
Record linkage, independent blind assessment, previously validated/reliable measures	2
Independent assessment un-blinded; self-report, novel measures (validation/ reliability data provided	1
Novel measures (no validation/reliability tests) or assessment of outcome not described	0
IV. Adequacy of follow-up and/or were all patients included	
Yes (follow-up > 95%) of patients or > 95% of all patients included	2
Reasonable follow-up of all patients or all patients included (>80%)	1
\leq 80% of patients /included patients followed-up, not described or not relevant	0
V. Adequacy of adjustment for confounding: (matching, stratification, multivariate at	nalysis
Yes	2
Not clear or not applicable	1
No	0
VI. If there was adjustment for residual confounding	
Study comprehensively controls for age and additional risk factors	2
Study controls for age and most plausible additional factors	1
Minimum matching or adjustment for plausible prognostic variables; no adjustment	0
VII. Attrition (missing data): If a concern was missing data handled appropriately	
Yes	2
Not clear or not applicable	1
No	0
VIII. Statistical methods adequate or appropriate and sufficiently described	
Yes	2
Not clear or not applicable	1
No	0
IX. Data presentation	
Examples of data presented allows clear understanding of data analysis and interpretation	2
Examples provided but do not present a clear interpretation of data	1
Very little data presented or incomplete recording	0

Additional file 3: Excluded studies with reasons for exclusion

Study Reference	Reason for Exclusion
Achat et al 2005 ¹	No results by residential location of women or for rural women
Andreeva & Pokhrel 2013 ²	Does not assess one of the considered clinical questions
Ahern et al 2015 ³	No results by residential location of women or for rural women
Azzopardi <i>et al</i> 2014 ⁴	No results by residential location of women or for rural women
Banks <i>et al</i> 2014 ⁵	No results specifically for female breast cancer patients
Banks <i>et al</i> 2010 ⁶	No results specifically for female breast cancer patients
Barratt <i>et al</i> 1999 ⁷	No results by residential location or for rural women in target screening age group
Beckmann et al 2011 8	Does not assess one of the considered clinical questions
Bell et al 2009 9	Does not assess one of the considered clinical questions
Bessen et al 2014 10	Does not assess one of the considered clinical questions
Bessen & Karnon 2014 11	Does not assess one of the considered clinical questions
Boyages et al 2010 12	Does not assess one of the considered clinical questions
Brennan & Spillane 2013 ¹³	Review
Brennan & Houssami 2006 ¹⁴	Does not assess one of the considered clinical questions
Brennan et al 2014 15	Review
Brennan <i>et al</i> 2011 ¹⁶	Does not assess one of the considered clinical questions
Brennan <i>et al</i> 2011 ¹⁷	Opinion piece
Brennan <i>et al</i> 2010 ¹⁸	Survey of health professionals rather than women with breast cancer
Brennan <i>et al</i> 2010 ¹⁹	Does not assess one of the considered clinical questions
Brown <i>et al</i> 2013 ²⁰	No results by residential location or for rural women in target screening age group
Buckley et al 2017 ²¹	Does not assess one of the considered clinical questions
Buckley <i>et al</i> 2014 ²²	Does not assess one of the considered clinical questions
Budden <i>et al</i> 2007 ²³	Does not assess one of the considered clinical questions
Budden et al 2003 ²⁴	Does not assess one of the considered clinical questions
Butler-Henderson <i>et al</i> 2014 ²⁵	In situ and not invasive breast cancer
Canfell 2014 ²⁶	Review
Carrick <i>et al</i> 1998 ²⁷	Opinion piece
Chavez-Macgregor & Hortobagyi	Opinion piece
2011 28	
Chin et al 2008 ²⁹	In situ and not invasive breast cancer
Chisholm et al 2000 30	Does not assess one of the considered clinical questions
Clarke 2002 31	Economic analysis; Does not assess one of the considered clinical questions
Clarke 1998 ³²	Economic analysis: Does not assess one of the considered clinical questions
Clover <i>et al</i> 1996 33	No results by residential location or for rural women in target screening age group
Cockburn et al 1997 34	No results by residential location or for rural women in target screening age group
Cockburn et al 1991 35	No results by residential location or for rural women in target screening age group
Coleman et al 2011 36	A comparative study across countries only
Coleman et al 2008 37	A comparative study across countries only
Craft et al 2010 38	No information by patient's residential location; only by treatment centre location
Cramb <i>et al</i> 2012 ³⁹	Does not assess one of the considered clinical questions
Cramb <i>et al</i> 2011 ⁴⁰	No results specifically for female breast cancer patients
Crombie et al 2005 41	No results by residential location of women or for rural women
Davey et al 2008 42	Does not assess one of the considered clinical questions
Delpizzo 1995 ⁴³	Does not assess one of the considered clinical questions
Dowling et al 2014 44	Does not assess one of the considered clinical questions
Emery <i>et al</i> 2013 ⁴⁵	No results specifically for female breast cancer patients
Emery 2010 ⁴⁶	Conference abstract
Fisher <i>et al</i> 2014 ⁴⁷	Not Australian-based
Fong <i>et al</i> 2012 ⁴⁸	A comparative study across countries only

Study Reference	Reason for Exclusion
Fong <i>et al</i> 2012 ⁴⁹	A comparative study across countries only
Frensham et al 2014 50	No results specifically for female breast cancer patients
Furnival 2004 51	Editorial
Furnival 1997 52	Editorial
Giles et al 2010 53	Methodological paper
Goldsbury et al 2012 54	Not breast cancer
Green et al 2013 55	Conference abstract
Halkett et al 2014 56	Study protocol
Halkett et al 2006 ⁵⁷	No results by residential location of women or for rural women
Harden et al 2014 58	Conference abstract
Harrison et al 2008 59	No results by residential location of women or for rural women
Hayes et al 2010 60	No results by residential location of women or for rural women
Heathcote & Armstrong 2007 ⁶¹	Review
Hersch et al 2014 62	Study protocol
Heywood et al 1994 63	Does not assess one of the considered clinical questions
Hunt <i>et al</i> 2001 ⁶⁴	Does not assess one of the considered clinical questions
Hyndman & Holman 2000 65	Does not assess one of the considered clinical questions
Hyndman et al 1997 66	Does not assess one of the considered clinical questions
Ingram <i>et al</i> 2005 ⁶⁷	No information by patient's residential location; only by surgical caseload
Jones 2004 ⁶⁸	Opinion piece
Jong <i>et al</i> 2005 ⁶⁹	Opinion piece
Kavanagh <i>et al</i> 1999 ⁷⁰	Does not assess one of the considered clinical questions
Kiely <i>et al</i> 2013 ⁷¹	Does not assess one of the considered clinical questions
Kiely <i>et al</i> 2010 ⁷²	Includes women with high breast cancer risk, no results by residential location
Kremser et al 2008 73	Does not assess one of the considered clinical questions
Kricker 1998 74	Review
Kricker et al 2009 75	No results by residential location of women or for rural women
Kricker et al 2008 76	Does not assess one of the considered clinical questions
Kwok & White 2011 77	Does not assess one of the considered clinical questions
Lawler et al 2012 78	Does not assess one of the considered clinical questions
Llewellyn et al 2011 79	Does not assess one of the considered clinical questions
Lobb <i>et al</i> 2002 80	Includes women with high breast cancer risk, no results by residential location
Lopez et al 2013 81	Not breast cancer
Lu <i>et al</i> 2013 ⁸²	Does not assess one of the considered clinical questions
Luke <i>et al</i> 2006 83	Does not assess one of the considered clinical questions
Luke <i>et al</i> 2003 84	No results specifically for female breast cancer patients
Magiros et al 2001 85	Does not assess one of the considered clinical questions
Marsh <i>et al</i> 2008 86	No information by patient's residential location; only by treatment centre location
Mauad <i>et al</i> 2009 87	Not Australian-based
McCredie et al 1995 88	Review
McMichael et al 2000 89	Does not assess one of the considered clinical questions
Moorin & Holman 2006 90	Does not assess one of the considered clinical questions
Moran & Warren-Forward 2011 91	Does not assess one of the considered clinical questions
Morley et al 2010 92	Only included women from urban areas
Morrell et al 2012 93	Does not assess one of the considered clinical questions
Ogunsiji <i>et al</i> 2013 ⁹⁴	Does not assess one of the considered clinical questions
Paddison &Yip 2010 95	Not breast cancer
Page <i>et al</i> 2006 96	Does not assess one of the considered clinical questions
Peters 2012 97	Does not assess one of the considered clinical questions
Protani et al 2012 98	Does not assess one of the considered clinical questions

	D. C. E. L.
Study Reference	Reason for Exclusion
Richardson 2013 99	Opinion piece
Roder <i>et al</i> 2014 100	Does not assess one of the considered clinical questions
Roder <i>et al</i> 2011 ¹⁰¹	Conference abstract
Rychetnik et al 2013 102	Editorial
Sandelin et al 2003 103	Does not assess one of the considered clinical questions
Sharma et al 2016 ¹⁰⁴	No results specifically for female breast cancer patients
Sharplin et al 2014 105	No results specifically for female breast cancer patients
Shugg <i>et al</i> 2002 ¹⁰⁶	Ductal carcinoma and not invasive breast cancer
Smith 2012 ¹⁰⁷	Review
Somogyi <i>et al</i> 2015 108	No information by patient's residential location; only by treatment centre location
Speedy & Hase 2000 109	Does not assess one of the considered clinical questions
Spillane <i>et al</i> 1999 110	No outcomes by patient's residential location; only by treatment centre location
Spillane et al 2001 111	No results by residential location of women or for rural women
Spilsbury et al 2005 112	Does not assess one of the considered clinical questions
Stanbury et al 2016 113	No results by residential location of women or for rural women
Stanton <i>et al</i> 1995 114	Does not assess one of the considered clinical questions
Sullivan et al 2004 115	Does not assess one of the considered clinical questions
Taylor et al 2003 116	No results by residential location of women or for rural women
Taylor <i>et al</i> 1999 117	Only included women from urban areas
Thewes et al 2003 118	Review
Thiruvarudchelvan et al 2010 119	Does not assess one of the considered clinical questions
Turnbull <i>et al</i> 1994 120	Does not assess one of the considered clinical questions
Villanueva et al 2008 121	No results by residential location of women or for rural women
Ward et al 2000 122	Does not assess one of the considered clinical questions
Weller 1998 123	Not breast cancer
Whitfield et al 2012 124	No information by patient's residential location; only by treatment centre location
Wilcoxon et al 2011 125	No results specifically for female breast cancer patients
Willis 2004 ¹²⁶	Looks at women outside the target age group for screening
Willis & Baxter 2003 127	Looks at women outside the target age group for screening
Winch <i>et al</i> 2015 ¹²⁸	Does not assess one of the considered clinical questions
Winefield et al 2004 129	Does not assess one of the considered clinical questions
Wong <i>et al</i> 2014 ¹³⁰	No results by residential location of women or for rural women
Woods <i>et al</i> 2010 ¹³¹	A comparative study across countries only
Yelland <i>et al</i> 1991 132	No results by residential location of women or for rural women
Youl <i>et al</i> 2016 ¹³³	Does not assess one of the considered clinical questions
Youl et al 2011 134	Study protocol
Yu et al 2006 135	Does not assess one of the considered clinical questions
Zardawi <i>et al</i> 1999 ¹³⁶	Does not assess one of the considered clinical questions
Zilliacus <i>et al</i> 2010 ¹³⁷	Genetic counselling

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${\bf Additional\ file\ 4\ Detailed\ characteristics\ of\ the\ included\ studies\ by\ three\ key\ themes.}$

Table 1. Detailed characteristics of included studies on survival outcomes by residential location

Study	Location ¹	Design	Source	Period (follow- up)	Sample ²	Outcomes	Analysis	Key findings
AIHW 2013 ¹	National	Cohort	ACD	1982-2007 (end 2010)	NS	5-year relative survival	Relative survival	Poorer survival for non-metropoltan women (84% versus 90% metropolitan). No adjusted estimates.
Bonnet <i>et al</i> 1990 ²	SA	Cohort	SA CR	1980-1986 (end 1988)	2,565	5-year relative survival	Proportional hazards regression	Poorer unadjusted (74% versus 76-78% metropolitan) and adjusted ³ survival (2-9 times higher mortality risk) for non-metropolitan women.
Chen <i>et al</i> 2015 ³	NSW	Cohort	NSW CCR	2000-2008	36,867	5-year BC survival	Kaplan-Meir, Cox regression	Poorer survival for outer regional women with regional (82% versus 86% metropolitan) and distant (33% versus 44%) disease. Also poorer adjusted ⁴ survival (regional: 22%; distant: 30% higher BC mortality).
Clayforth et al 2007 ⁴	WA	Cohort	WA CR	1989, 1994, 1999 (end 2005)	1,729	5-year overall survival	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women (79% versus 85% metropolitan). Metropolitan women had better adjusted ⁵ survival (30% lower mortality). ⁵
Cramb et al 2012 ⁵	Qld	Cohort	Qld CR	1996-2007	25,202	5-year relative survival	Bayesian spatial regression	Poorer survival for women living >6 hours from a radiation facility (83% versus 86% living <2 hours). No difference after adjustment. ⁶
Cramb <i>et al</i> 2016a ⁶	Qld	Cohort	Qld CR	1997-2011	NS	5-year relative survival	Bayesian spatial regression	Poorer survival for non-metropolitan women after adjustment. ⁷
Cramb <i>et al</i> 2016b ⁷	Qld	Cohort	Qld CR	1997-2011	34,231	5-year relative survival	Bayesian spatial regression	Poorer survival for non-metropolitan women after adjustment. ⁷
Cramb <i>et al</i> 2017 ⁸	Qld	Cohort	Qld CR	1997-2004 (end 2005); 2005-2012 (end 2013)	38,204, aged 15-89 years	5-year relative survival	Bayesian spatial regression	Poorer age-adjusted survival for non-metropolitan women.
Dasgupta <i>et al</i> 2012 ⁹	Qld	Cohort	Qld CR	1997-2006 (end 2007)	18,568, first primary, aged 30-79 years	5-year BC survival	Kaplan-Meir, Multilevel regression	Poorer survival for non-metropolitan women (88% versus 91% metropolitan). No difference after adjustment. ⁸
Hall <i>et al</i> 2004a ¹⁰	WA	Cohort	WA Record Linkage Project	1991-2001	7,117, BC- surgery	5-year overall survival	Chi-square, Cox regression	Poorer survival for non-metropolitan women (78% versus 83% metropolitan). No difference after adjustment. ⁹
Hsieh <i>et al</i> 2014 ¹¹	Qld	Cohort	Qld CR, BS Qld	1997-2007 (end 2008)	23,766, aged <90 years	5-year relative survival	Bayesian spatial regression	Poorer unadjusted and adjusted survival for non-metropolitan women (relative excess risk of death 1.1-1.4). ¹⁰
Hsieh <i>et al</i> 2016a ¹²	Qld	Cohort	Qld CR, BS Qld	1997-2007 (end 2008)	23,766, aged <90 years	5-year relative survival	Bayesian spatial regression	Poorer survival for non-metropolitan women after adjustment. ¹¹
Hsieh <i>et al</i> 2016b ¹³	Qld	Cohort	Qld CR, BS Qld	1997-2007 (end 2008)	9,741, aged 40- 89 years, screened	5-year relative survival	Bayesian spatial regression	No difference in unadjusted and adjusted survival. 10
Mitchell <i>et al</i> 2006 ¹⁴	WA	Cohort	WA CR	1999 (end 2004)	899, first primary	5-year overall survival	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women (78% versus 87% metropolitan). No difference after adjustment. ¹²

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Study	Location ¹	Design	Source	Period (follow- up)	Sample ²	Outcomes	Analysis	Key findings
Roder <i>et al</i> 2012a ¹⁵	National	Cohort	National BS, CR's, record linkage	1991-2006	62,082, screeened	5-year overall & BC survival	Cox regression	Poorer survival for regional non-Indigenous (88-89% versus 90% metropolitan) and Indigenous women (75-79% versus 86%). No difference after adjustment. ¹³
Spilsbury <i>et al</i> 2005 ¹⁶	WA	Cohort	WA Record Linkage Project	1982-2000	11,445, BC- surgery	5-year relative & BC survival	Relative survival, Cox regression	Poorer survival for non-metropolitan women (82% versus 86% metropolitan). No difference after adjustment. ¹⁴
Supramaniam et al 2014 ¹⁷	NSW	Cohort	NSW CCR, NSW APDC, record linkage	2001-2007 (end 2008)	27,850, aged ≥18 years	5-year BC survival	Cox regression	Non-metropolitan women had (unadjusted) 11%-20% poorer survival than metropolitan women. No difference after adjustment. 15
Taylor 1997 ¹⁸	NSW	Cohort	NSW CCR	1980-1991 (end 1992)	25,793	5-year relative survival	Relative survival models	No differences in either unadjusted or adjusted ¹⁶ survival estimates.
Tervonen et al 2017 19	NSW	Cohort	NSW CCR	1980-2008 (end 2009)	88,768	5-year BC survival	Competing risk	Poorer unadjusted survival for non-metropolitan women. No difference after adjustment. ¹⁷
Tracey et al 2008 ²⁰	NSW	Cohort	NSW CCR	1980-2003 (end 2004)	59,731, known spread of disease	Case fatality: 5 and 10 years post-diagnosis	Kaplan-Meir, Cox regression	Poorer survival for non-metropolitan women. No difference after adjustment. ¹⁷
Yu et al 2015 ²¹	NSW	Cohort	NSW CCR	1987-2007 (end 2007)	63,757, aged 18-84 years	5-year relative survival	Relative survival models	Poorer survival for non-metropolitan women. Also 25% poorer adjusted ¹⁸ survival from 1997 onwards (non-localised disease only).
Wilkinson & Cameron 2004 ²²	SA	Cohort	SA CR	1977-1993 (to 2000)	NS PC	5-year BC survival	Survival percentages	Poorer survival for non-metropolitan women (73% versus 77% metropolitan). No adjusted estimates ancer Registry, CCR Central Cancer Registry, NS not stated

- National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia and WA Western Australia
- Female invasive breast cancers cases
- Adjusted for tumour size and nodal status.
- Adjusted for age at diagnosis and stratified by spread of disease (classified as localised, regional or distant).
- Adjusted for age and year at diagnosis, spread of disease, surgical caseload and treatment-related factors.
- Adjusted for age at diagnosis, spread of disease, distance to treatment and area-disadvantage.
- Adjusted for age at diagnosis and spread of disease.
- Adjusted for age at diagnosis, spread of disease, Indigenous status, demographics, and area-disadvantage.
- Adjusted for age and year at diagnosis, Indigenous status, demographics, comorbidities, area-disadvantage, hospital characteristics and surgical status.

- Adjusted for age at diagnosis, spread of disease, Indigenous status, demographics, detection methods and area-disadvantage
- Adjusted for age at diagnosis, spread of disease, Indigenous status, demographics and screening status.
- Adjusted for age at diagnosis, spread of disease, surgical caseload and treatment-related factors.
- 13. Adjusted for age at diagnosis, diagnostic period, Indigenous status and area-disadvantage.
- Adjusted for age at diagnosis, diagnostic period, Indigenous status, comorbidities, area-disadvantage, hospital type and treatment-related factors.
- Adjusted for age and year at diagnosis, spread of disease, Indigenous status, comorbidities, area-disadvantage and surgical status.
- Adjusted for age at diagnosis, spread of disease, follow-up interval and interactions between these variables.
- Adjusted for age at diagnosis, diagnostic period, spread of disease, area-disadvantage and country of birth.
- Adjusted for age at diagnosis, diagnostic period and area-disadvantage; stratified by spread of disease (classified as localised or non-localised).

Table 2. Characteristics of included studies on patient and tumour characteristics by residential location

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings
Roder <i>et al</i> 2013a ²³	National	Non- representative sample	NBCA database ³	1998-2010	30,299, early disease ⁴	Predictors of increasing residential remoteness	Chi-square, Logistic regression	Disadvantaged women (versus affluent) more likely to live in inner regional (10 times), outer regional (33 times) or remote (17 times) areas than metropolitan areas. Residential disadvantage a key predictor of increasing remoteness. ⁵
Roder <i>et al</i> 2014 ²⁴	National	Non- representative sample	NBCA database ³	1998-2010	30,299, early disease ⁴	Predictors of lower residential disadvantage	Chi-square, Logistic regression	Inner regional (5 times, versus metropolitan), outer regional (10 times) and remote women (13 times) more likely to live in disadvantaged than affluent regions. ⁶
Baade <i>et al</i> 2011 ²⁵	Qld	Cohort	Qld CR	1997-2006	18,568, aged 30-79 years, known tumour size and nodal status (if ≤20mm)	Stage ⁷	Multilevel logistic regression	Outer regional women (versus metropolitan) 13% more likely to have advanced disease.8
Bonnet <i>et al</i> 1990 ²	SA	Cohort	SA CR	1980-1986	1,171, known tumour size and nodal status	Tumour size, nodal status	Chi-square	No differences in tumour size or nodal status.
Dasgupta et al 2017a ²⁶	Qld	Cohort	Qld CR	1997-2014	38,706, aged at least 30 years, known tumour size and nodal status	Stage ⁷	Multilevel logistic regression	Women from less accessible areas (versus highly accessible) 18% more likely to have advanced disease. Trend analysis showed only limited evidence for reduction in disparity over time.
Depczynski, et al 2017 ²⁷	NSW	Record linkage	45 and Up study, NSW CR	2006-2009	726, aged at least 45 years, known spread of disease	Degree of spread ¹⁰	Chi-square, Logistic regression	No differences in degree of spread. ¹¹
Fox <i>et al</i> 2013 ²⁸	NSW	Medical chart reviews	4 medical centres	2008-2011	400, Stage 1-III, had adjuvant CT	Median tumour size	Mann- Whitney	No differences in tumour size.
Kok <i>et al</i> 2006 ²⁹	Vic	Retrospective cohort	BS Vic	1993-2000	5,294, screen-detected	Tumour size, nodal status	Chi-square	Non-metropolitan women (versus metropolitan) had larger tumours; no difference in nodal status.
Leung <i>et al</i> 2016 ³⁰	NSW, Qld, Vic	Record linkage	ALSWH NSW Vic & QLD CR's	1997-2011	195, aged 50-55 years, known spread of disease,	Stage ⁷	Logistic regression	No difference in stage. ¹²
Luke <i>et al</i> 2004 ³¹	SA	Cohort	SA CR	1997-2002	4,912, known tumour size	Tumour size	Mann- Whitney	No difference in tumour size
Lord <i>et al</i> 2012 ³²	NSW	Cohort	NSW CR	2001-2002	6,664, non-metastatic, known spread of disease	Degree of spread ¹³	Chi-square	No difference in degree of spread
Mitchell et al 2006 ¹⁴	WA	Cohort	WA CR	1999	899, first primary, histologically verified	Tumour size, grade, vascular invasion, nodal status	Chi-square	No differences in tumour size or other characteristics
Roder <i>et al</i> 2013b ³³	National	Non- representative sample	NBCA database ³	1998-2010	30,299, early disease ⁴	Tumour size, grade, nodal status, receptor status	Chi-square	Non-metropolitan women (versus metropolitan) 15% more likely to have larger tumours. No differences in other characteristics.

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Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings
Tracey <i>et al</i> 2008 ²⁰	NSW	Cohort	NSW CCR	1980-2003	59,731, known spread of disease	Degree of spread ¹³	Logistic regression	Metropolitan women 11% more likely to have regional disease than non-metropolitan women. ¹⁴ No difference for distant disease
Wilkinson & Cameron 2004 ²²	SA	Cohort	SA CR	1980-1998	NS	Proportion of tumours >20mm	Chi-square	No difference in tumour size

ALSWH Australian Longitudinal Study on Women's Health, BS BreastScreen, CR Cancer Registry, CCR Central Cancer Registry CT Chemotherapy, NBCA National Breast Cancer Audit Database, NS not stated

- 1. National: all states/territories; NSW: New South Wales; Qld: Queensland: SA: South Australia; Vic: Victoria and WA Western Australia
- Female invasive breast cancers cases
- 3. National Breast Cancer Audit Database covers about 60% of early (note 4) invasive female breast cancers diagnosed in Australia between 1998 and 2010.
- 4. Early disease defined as invasive tumours of ≤50mm size with either impalpable or palpable but not fixed lymph nodes and no evidence for distant metastases.
- 5. Adjusted for age at diagnosis, diagnostic period, area disadvantage, surgical caseload, hospital location and treatment-related factors.
- 6. Adjusted for diagnostic period, referral source, tumour laterality, ovarian ablation and hospital location.
- 7. Classified as early (≤20mm size, no evidence of nodal involvement) or advanced/late (>20mm size and/or positive nodal status, includes cases diagnosed due to metastatic disease)
- 8. Adjusted for age at diagnosis, diagnostic period, Indigenous status, demographics and area-disadvantage.
- 9. Adjusted for age and year at diagnosis, Indigenous status, clinical features, demographics and area-disadvantage.
- 10. Classified as localised (node-negative) or non-localised (regional or distant).
- 11. Adjusted for age at diagnosis, family history of cancer and demographics.
- 12. Adjusted for year of diagnosis and birth, demographics, menopausal status, hormone replacement therapy and area-disadvantage
- 13. Classified as localised (node-negative), regional (involves regional lymph nodes or adjacent tissues, includes locally advanced disease) or distant (metastatic disease).
- 14. Adjusted for age at diagnosis, diagnostic period, area-disadvantage and country of birth.



Table 3. Characteristics of included studies on diagnostic outcomes

Study	Location ¹	Design	Source	Period	Sample	Outcomes	Analysis	Key findings
Barratt <i>et al</i> 1997 ³⁴	National	Cross-sectional	Telephone directory	1996	1,035, aged 50-69 years, no breast cancer history	Self-reported screening history	Chi-square	No differences in screening rates.
Cockburn <i>et al</i> 1997 ³⁵	Vic	Cross-sectional	Local media, community groups	1995	180, aged 50-69 years, no screening 6-months	Utilization of a screening service	Logistic regression	No previous screening history, higher perceived breast cancer risk, lower education and knowledge of service location predictors of screening. ²
Leung <i>et al</i> 2014 ³⁶	National	Longitudinal prospective survey	ALSWH	2001- 2010	11,200, aged 50-55 years (2001)	Self-reported screening history, rescreening (within last two years)	Chi-square, Logistic regression	No differences in screening rates. ³ Non- metropolitan women (versus metropolitan) had poorer access to screening services and were 25- 63% more likely to be rescreened. ³
Leung <i>et al</i> 2015 ³⁷	National	Longitudinal prospective survey	ALSWH	2010	10,011, aged 59-64 years (2010)	Self-reported screening history, rescreening (within last two years)	Chi-square, Logistic regression	No differences in screening rates. Non-metropolitan women (versus metropolitan) were 15% more likely to be rescreened.
Schofield et al 1994 ³⁸	Vic	Random sampling	Electoral lists (target area)	1988- 1990	668, aged 50-69 years	Utilization of a single screening service	Logistic regression	Women who lived within 10-20 km (versus < 2km) of the service 43% less likely to be screened. ⁵
Siapush & Singh 2002 ³⁹	National	Multistage sampling	ANHS	1995	10,179, aged ≥18 years	Self-reported screening history, rescreening (1 year)	Logistic regression	Non-metropolitan women (versus metropolitan) 39% more likely to have no screening history and 20% more likely to not be rescreened. ⁶
Sullivan et al 2003 ⁴⁰	WA	Record linkage	Disability Services database, WA CR, BS WA	1982- 2000	380, aged 50-69 years, known intellectual disability	Utilization of screening service	Logistic regression	Non-metropolitan women (versus metropolitan) 2 times more likely to be screeened. ⁷
Weber <i>et al</i> 2014 ⁴¹	NSW	Cohort	Medicare Australia	2006- 2010	101,063 (76% Australian, 24% immigrant), aged ≥50 years	Self-reported screening history	Poisson regression	Non-metropolitan Australian-born women (versus metropolitan) 2% more likely to be screeened.8 No difference for immigrant women.
Hughes <i>et al</i> 2014 ⁴²	WA	Retrospective cohort	BS WA	1999- 2008	NS, aged 50-67 years, had screening history	Rescreening (within 27 months)	Not stated	No differences in rescreening rates
O'Byrne <i>et al</i> 2000 ⁴³	Vic	Retrospective cohort	BS Vic	1995- 1996	121,889, aged 50–69 years, had screening history	Rescreening (within 27 months)	Logistic regression	Non-metropolitan women (versus metropolitan) women 13-24% more likely to be rescreened. ⁹

ALSWH Australian Longitudinal Study on Women's Health, ANHS Australian National Health Survey, BS BreastScreen, CR Cancer Registry

- 1. National: all states/territories; NSW: New South Wales; Vic: Victoria and WA Western Australia
- 2. Adjusted for screening history, perceived breast cancer risk, screening awareness and barriers, knowledge of service location, intention to attend and socio-demographics
- 3. Adjusted for time and interaction between time and residential area.
- 4. Adjusted for age and area-disadvantage.
- 5. Adjusted for intention to attend, breast cancer related factors, screening awaren, barriers and concerns, other preventive behaviours and demographics.
- 6. Adjusted for age, demographics and area-disadvantage.
- 7. Adjusted for age, demographics and health-status related factors.
- 8. Adjusted for age, demographics and hormone replacement therapy; stratified by country of birth .
- 9. Adjusted for age, Indigenous status, demographics, area-disadvantage and clinical factors related to initial screening.

Table 4. Characteristics of included studies on treatment outcomes

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings		
Adelson et al 1997 ⁴⁴	NSW	Retrospective record linkage	NSW CCR, ISC	1991-1992	4,038, known spread disease, BC-surgery	BCS versus MST	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 2 times more likely to have MST (localized disease); no difference for metastatic disease. ³		
Ahern <i>et al</i> 2015 ⁴⁵	National	Cross-sectional	Two national databases	2013	325, aged at least 18 years, BC diagnosis 6-30 months ago	RT, CT, HT, BR	Chi-square	No differences in receipt of surgery or adjuvant therapies.		
Ahern <i>et al</i> 2016 ⁴⁶	National	Cross-sectional	Two national databases	2013	902, aged at least 18 years, post active treatment	Interactions with BCN, CT	Chi-square	No differences in receipt of BCN care or CT		
Azzopardi et al 2014 ⁴⁷	National	Clinical audit	NBCA database ⁴	1998-2012	21,643, early disease ⁵	BCS versus MST, adjuvant RT	Chi-square (surgery), Logistic regression (RT)	Proportions of BCS decreased and MST increased with increasing remoteness Women from areas lacking a RT facility (versus RT facility present, 23%) and nonmetropolitan women (versus metropolitan, 20%) less likely to have RT. ⁶		
Baade <i>et al</i> 2016 ⁴⁸	Qld	Cohort	Qld CR, Qld HAPDC, record linkage	1997-2011	11,631, aged at least 20 years, localised disease ⁷ , first primary BC, BC- surgery	BCS	Logistic regression	Women from less accessible areas (versus highly accessible) less likely to have BCS. Trend analysis showed some evidence for temporal reduction in disparity, but inequalities remained. Women living in more accessible areas more likely to attend high volume hospitals (≥100 cases per year).		
Bell <i>et al</i> 2012 ⁴⁹	Vic	Longitudinal cohort,	Health & Wellbeing After BC study	2004-2006	366, prior unilateral MST, known BR status	BR	Logistic Regression	Non-metropolitan women (versus metropolitan) 73% less likely to have BR.9		
Budden <i>et al</i> 2014 ⁵⁰	Qld (3 regional areas)	Cross-sectional	Local surgeons	NS	104, Stage 1-IIA, MST or BCS/RT	Satisfaction treatment decision	Chi-square	90% women satisfied with decision process		
Campbell et al 2006 ⁵¹	National (not Tas)	Cross-sectional	State Cancer Registries	1997	544, early disease	Systematic SBN care	Chi-square	No differences in receipt of systematic SBN care		
Chong <i>et al</i> 2015 ⁵²	National	Clinical audit	NBCA database ⁴	2008-2010	18,737, early disease ⁵	SNB	Logistic Regression	Non-metropolitan women (versus metropolitan) less likely to have SNB. ¹⁰		
Collins et al 2017 ⁵³	Vic (one regional area)	Cohort	ECO Barwon SW CR	2009-2014	1,213, early disease	BCS versus MST	Chi-square, Logistic regression	Women who lived ≥100-200 km (versus <100 km) of a radiotherapy centre were 1.6 times more likely to have MST. 11 No difference for those living more than 200 km away		
Craft <i>et al</i> 1997 ⁵⁴	National	Retrospective survey	Medicare Australia	1993	4,683, had BC- surgery	BCS, AS	Chi-square	Non-metropolitan women (versus metropolitan) had lower BCS (34% versus 42%); no differences in AS rates		
Dasgupta et al 2017b ⁵⁵	Qld	Cohort	Qld CR, Qld HAPDC, record linkage	1st July 2008-31st December 2012	5,577, aged at least 20 years, early disease ¹² , first primary BC, prior BCS or MST	SNB versus AS	Logistic regression	Women from less accessible areas (versus highly accessible) 39-58% less likely to have SNB. ¹³ Trend analysis showed no evidence for temporal eduction in geographical disparities.		

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings
Dasgupta et al 2017c ⁵⁶	Qld	Cohort	Qld CR, Qld HAPDC, record linkage	1997-2012	4,104, aged at least 20 years, localised disease ⁷ , first primary BC, prior MST	BR	Logistic regression	Women from less accessible areas (versus highly accessible) 27-74% less likely to have post-mastectomy BR. ¹⁴ Trend analysis showed that the geographical disparity had reduced over time.
Eley <i>et al</i> 2008 ⁵⁷	Qld (one region)	Cross-sectional	Local BCN	2005-2006	51, aged 38-79 years, post active treatment	Interactions with BCN	Frequencies	BCN valuable source of treatment-related information (86% sampled women) and help during decision-process (71%).
Flitcroft <i>et al</i> 2016 ⁵⁸	National	Clinical audit	NBCA database ⁴	2013	3,786, aged at least 20 years, early disease ⁵ , prior MST	BR	Chi-square	Non-metropolitan women (versus metropolitan) less likely to have BR
Fox <i>et al</i> 2013 ²⁸	NSW	Medical chart reviews	4 medical centres	2008-2011	400, non-metastatic, had adjuvant CT	Delays, CT finish	Chi-square, Mann- Whitney	Non-metropolitan women (versus metropolitan) more likely to have longer delays in consultation and starting CT and to complete CT course (90% versus 82%).
Hall & Holman 2003 ⁵⁹	WA	Cohort	WA Record Linkage Project	1991-2000	7,303, prior MST or BCS	BR (yes/no)	Chi-square, Cox regression	No differences in BR rates. ¹⁵
Hall <i>et al</i> 2004b ⁶⁰	WA	Cohort	WA Record Linkage Project	1991-2000	7,304, BC-surgery	BCS versus MST	Chi-square, Logistic regression	No differences in surgical patterns. 16
Hsieh <i>et al</i> 2015 ⁶¹	Qld	Cohirt	Qld CR, BS Qld, record linkage	1997-2008	6,357 aged 40-89, screen-detected BC	adjuvant RT, CT, HT	Bayesian shared spatial component model	Women living >4 or more hours from a radiation facility were 59% less likely to have adjuvant RT. ¹⁷ No differences for CT or HT
Hill <i>et al</i> 1994 ⁶²	Vic	Population-based survey	Vic CR	1990	856, BC-surgery	BCS, adjuvant RT, CT, HT, Referral	Chi-square, ANOVA, Student t-test	Non-metropolitan women (versus metropolitan) less likely to have BCS (33% versus 46%); no differences in adjuvant therapies (no quantitative data) or medical oncologist referrals. Non-metropolitan surgeons less likely to refer patients to radiation oncologists (28% versus 43%).
Kok <i>et al</i> 2006 ²⁹	Vic	Retrospective cohort	BS Vic	1993-2000	5,294 screen- detected	BCS versus MST, adjuvant RT	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 58% less likely to have BCS and 27% less likely to have post-BCS RT. ¹⁸
Koshy <i>et al</i> 2005 ⁶³	NSW, ACT	Prospective audit	Pathology reports, medical charts, clinicians	1997-2002	1,069, non- metastatic, BC- surgery	BCS versus MST	Chi-square	No differences in surgical patterns.
Kricker <i>et al</i> 2001 ⁶⁴	NSW	Cohort	NSW CCR, ISC record linkage	1992, 1995	2,020 or 2,883, BC- surgery	BCS versus MST, AS	Logistic regression	No differences in surgical patterns or AS rates. ¹⁹
Lai <i>et al</i> 2007 ⁶⁵	WA	Cohort/	WA Record Linkage Project	1995-1999	2,703, BC-surgery	Unplanned hospital readmission	Survival model	Metropolitan women (versus non-metropolitan) 10% lower unplanned readmission (within 42 days of initial surgery) rates. ¹⁸

Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings
Lam et al 2015 ⁶⁶	NSW (one region)	Cross-sectional	Local surgeons and nurses	2010-2014	574, early disease ⁵ , BC-surgery	BCS	Chi-square	BC rates increased by 9% when local publicly funded radiotherapy became available in 2013 compared to earlier years when only options were local private or publicly funded out-of-area services.
Martin <i>et al</i> 2006 ⁶⁷	WA	Cohort/	WA Record Linkage Project	1990-1999	2,713, first primary BC, BC-surgery	BCS versus MST	Logistic regression	Non-metropolitan women (versus metropolitan) more likely to have MST. ²⁰
Mastaglia & Kristjanson 2001 ⁶⁸	WA	Cross-sectional	WA CR	1996-1997	160, Stage I-II, BC- surgery	BCS versus MRM	Chi-square	Non-metropolitan women more likely to have MRM than BCS (71% versus 36% metropolitan).
Mitchell et al 2006 ¹⁴	WA	Cohort	WA CR	1999	899 (692 HR+) histologically verified	BCS, adjuvant RT, CT, HT, High (>=20 cases/year) caseload surgeon	Chi-square	Non-metropolitan women (versus metropolitan) less likely to have BCS (42% versus 59%), RT (43% versus 55%,), HT (64% versus 70%, if HR +, 75% versus 85%,) or high caseload surgical care (70% versus 86%); no difference in CT.
Morris <i>et al</i> 2012 ⁶⁹	National	Audit	NBCA, NSW CCR, Vic CR, MBS	2008 (last 6 months)	1,334 (NBCA), 1,359 (NSW), 1,267 (Vic), ≤30mm size	SNB	z-tests (pooled)	Non-metropolitan women less likely to have SNB (NCBA 66% versus 82% metropolitan; NSW 76% versus 86%; Vic 65% versus 81%).
Ristevski <i>et al</i> 2012 ⁷⁰	Vic (one regional area)	Cross-sectional	Local surgeons and nurses	NS	70, first primary BC, early disease ⁵ , ≥six weeks post-surgery	Satisfaction, Referral	Descriptive, Fischer's exact test	97% of sample satisfied with treatment decision process regardless of surgical procedure. 42% referred to other health professionals/service before surgery.
Roder <i>et al</i> 2013a ²³	National	Non- representative sample	NBCA database ⁴	1998-2010	30,299, early disease ⁵ ,	BCS versus MST, adjuvant RT, CT, Low (<=10 cases/year) caseload surgeon	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) less likely to have BCS (6%) or RT after BCS (7%) but more likely to have CT (10%), care at regional (4-31% versus major city) or remote centres (7 times) and low caseload care (9%). ²¹
Roder <i>et al</i> 2013b ³³	National	Non- representative sample	NBCA database ⁴	1998-2010	30,299, early disease ⁵	BCS versus MST, Low (<=10 cases/year) caseload surgeon	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) more likely to have MST (5-9 times, adjusted ²²) Low surgical caseload predictor of treatment outside major cities and higher MST.)
Roder <i>et al</i> 2013c ⁷¹	National	Non- representative sample	NBCA database ⁴	1998-2010	12,207, early disease ⁵ , prior MST,	IBR versus delayed or no BR	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 13% less likely to have IBR Metropolitan rather than inner regional treatment centre and high (≥11 cases/year) surgical caseload predictors of IBR. ²³
Roder <i>et al</i> 2012b ⁷²	National	Non- representative sample	NBCA database ⁴	1998-2005	36,775, early disease ⁵	Declining recommended treatment	Chi-square, Logistic regression	Women treated at non-metropolitan centres and low surgical caseload (≤20 cases/year) were more likely to decline BCS, RT, MST, AS or CT (caseload only,); HT (location only). ²⁴
Thompson et al 2008 ⁷³	Qld	Cohort	Qld CR, Qld HAPDC, record linkage	2004	1,274, early disease ⁵	MST, AS	Chi-square, Logistic regression	Non-metropolitan women (versus metropolitan) 2 times more likely to have MST, no differences in AS rates. ²⁵

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Study	Location ¹	Design	Source	Period	Sample ²	Outcomes	Analysis	Key findings
Tulloh & Goldsworthy 1997 ⁷⁴	Vic	Medical chart reviews	Single rural centre	1992-1995	28	BCS versus MST	Descriptive	Rural setting no impediment to BCS (68%) or a multidisciplinary approach (93%).

AS axillary surgery (lymph nodes), BC Breast Cancer, BCN breast cancer nurse, BCS breast conservation surgery, BR breast reconstruction, BS BreastScreen, CR Cancer Registry, CCR Central Cancer Registry, CT chemotherapy, HAPDC Hospital Admitted Patient Data Collection, HR hormone receptor, HT hormone therapy, IBR immediate breast reconstruction, ISC Inpatient Statistics Collection, MRM modified radical mastectomy, MST mastectomy, NBCA National Breast Cancer Audit (also called BOA, Breast Surgeons ANZ Quality Audit), SBN specialist breast nurse, SE South-East, SNB sentinel node biopsy, RT adjuvant radiotherapy

- 1. National: all states/territories; ACT: Australian Capital Territory; NSW: New South Wales; Qld: Queensland: SA: South Australia; Vic: Victoria and WA Western Australia
- 2. Female invasive breast cancers cases
- Adjusted for age at diagnosis, spread of disease, interaction between degree of spread and residential location.
- 4. National Breast Cancer Audit Database covers about 60% of early invasive female breast cancers diagnosed in Australia between 1998 and 2010.
- Early disease defined as invasive tumours of ≤ 50mm size with either impalpable or palpable but not fixed lymph nodes and no evidence for distant metastases.
- Adjusted for presence/absence of a radiotherapy facility in the same postcode as residential location of patient.
- 7. Localised disease defined as invasive tumours of <20mm size with no evidence of nodal involvemen or metastases.
- 8. Adjusted for age and year at diagnosis, Indigenous status, demographics, clinical features, comorbidities, area-disadvantage, hospital type and surgical caseload.
- 9. Adjusted for age at diagnosis, demographics and radiotherapy.
- 10. Adjusted for age at diagnosis, health insurance status and surgical caseload.
- 11. Adjusted for age at diagnosis, tumour size and area disadvantage
- 12. Early disease defined as invasive tumours of ≤ 50mm size with no evidence of nodal involvement or metastases.
- 13. Adjusted for age and year at diagnosis, tumour size, initial surgical procedure, area-disadvantage, hospital type and surgical caseload.
- 14. Adjusted for age and year of diagnosis, Indigenous status, tumour size, area-disadvantage, hospital type and surgical caseload.
- 15. Adjusted for age at diagnosis, diagnostic period, Indigenous status, demographics, comorbidities, area-disadvantage and hospital related factors.
- 16. Adjusted for age at diagnosis, Indigenous status, demographics, clinical features, first screen diagnosis and area-disadvantage.
- 17. Adjusted for age at diagnostic period, demographics, clinical features, area-disadvantage, symptom status, cancer history and surgical caseload
- 18. Adjusted for age at diagnosis, area-disadvantage and country of birth.
- 19. Adjusted for age at diagnosis, clinical features, initial surgical procedure, health insurance status, country of birth and interactions between these variables.
- 20. Adjusted for age at diagnosis, clinical features, Indigenous status and demographics.
- 21. Adjusted for diagnostic period, area disadvantage and hospital location.
- 22. Adjusted for tumour size
- 23. Adjusted for age and year at diagnosis, clinical features, area-disadvantage, referral source, health insurance status, surgical caseload and treatment-related factors.
- 24. Adjusted for age at diagnosis, clinical features, hospital location, health insurance status and surgical caseload
- 25. Adjusted for age at diagnosis, tumour size, comorbidities, hospital type and surgical caseload.

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
8 Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5, Table 1
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NR
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	NR
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
2 Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NR
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., 12) for each meta-analysis com/site/about/guidelines.xhtml	7



PRISMA 2009 Checklist

		Page 1 of 2	
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NR
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Tables 2- 6 (Pages 20-26)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7-8, Tables 2- 6 (Pages 20-26)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-12, Tables 2- 6 (Pages 20-26)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NR
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NR
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NR
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
		Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-16

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PRISMA 2009 Checklist

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17
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For more informatio. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097